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THE INCIDENCE OF GENETIC DISORDERS IN CHILDREN AND YOUNG ADULTS

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ABSTRACT

One necessary prerequisite before any possible increase in genetic load from mutagens can be estimated is baseline information on the magnitude of genetically-caused ill health already present in the population. The present study utilizes the data base of an ongoing population-based Registry with multiple sources of ascertainment to estimate the present population load from genetic disease. It was found that 4.9% of liveborn individuals below 25 can be expected to have genetic or partly genetic diseases. This was composed of single-gene disorders (autosomal dominant, autosomal recessive and X-linked recessive), chromosomal anomalies and multifactorial disorders (including those present at birth and those later in onset). Since previous studies have usually considered all congenital anomalies (ICD 740-759) as part of the genetic load, data are also presented separately for this category to facilitate comparison with earlier studies.

These new data should represent a better estimate of the genetic load in the population than previous studies.

RÉSUMÉ

Avant de pouvoir estimer l'augmentation de la fréquence des anomalies génétiques dues aux mutagènes, il est nécessaire de connaître la fréquence actuelle des maladies génétiques dans la population. Cette étude utilise la base de données d'un registre de la population qui tient compte de sources multiples pour estimer la fréquence des maladies génétiques dans la population. D'après ces données, on peut s'attendre à ce que 4,9 % des individus âgés de moins de 25 ans soient atteints de maladies génétiques ou partiellement génétiques. Ce taux de maladie comprend les désordres causés par un seul gène (autosomique dominant, autosomique récessif et X-lié récessif), les anomalies de chromosomes et les désordres multifactoriels (y compris ceux présents à la naissance et ceux qui se développent plus tard). Parce que les études précédentes ont considéré toutes anomalies congénitales (CMI-740-759) comme faisant partie du patrimoine génétique, on présente ici séparément des données pour cette catégorie pour faciliter la comparaison avec les études antérieures.

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CHAPTER 1 INTRODUCTION

Current estimates of the genetic risks from exposures to ionizing radiation are based on two kinds of data, a) incidence rates in humans for the genetic diseases that are believed to be present in the population due to mutations of natural origin, and b) radiation induced mutation rates. These mutation rates are derived from work with experimental animals, and also from exceedingly limited and largely negative data from the offspring of atomic bomb survivors[32]. The present study seeks to augment existing data on the incidence of hereditary and partially hereditary disease in man.

The idea that exposure to ionizing radiation could contribute substantially to an existing social "load" of harmful genes and the hereditary diseases they cause was given special emphasis in 1950 by H.J. Muller[24]. This belief together with the indications for a linear non-threshold dose response relationship for radiation-induced mutation in lower organisms, resulted in a lowering of the legal limits to occupational radiation exposures in virtually all developed countries in the late 1950's. Unfortunately, quantitative estimates of the amount of genetic harm to be expected from a given level of exposure are exceedingly unsatisfactory. Rigorous data in humans concerning the magnitude of the induced genetic harm are difficult to obtain. Even so, it is possible to improve existing data on which the genetic estimates are based. One needed ingredient is better information on the magnitude of the public health burden from those genetic diseases now existing in our population. It is most appropriate to evaluate this information by various categories of genetic disease, as these would be expected to differ in their responses to an artificially induced elevation of the mutation rate.

Information of this sort has come in the past partly from special surveys and partly from population based registries. These two kinds of source tend to complement one another. In the past, valuable information has been obtained from the British Columbia Health Surveillance Registry for the purposes of genetic risk assessment[36,37], and this information has been quoted in most of the succeeding reports from official committees concerned with the genetic aspects of radiological protection[41,42]. The British Columbia Registry has grown substantially since the earlier study, and in addition further categorization of the data by etiology is possible. This means that analysis of the updated data should allow more accurate estimates of population load from genetic disease. Relevant data obtained from the current records of the Registry are the subject of the present account.

The Health Surveillance Registry of British Columbia[13] records and classifies cases of handicapping conditions, congenital anomalies and familial disorders in the

population of that Province. The information is provided by a number of government agencies concerned with health, rehabilitation and human resources, and by hospitals, treatment and rehabilitation centres, voluntary agencies, physicians and the vital registration system (see Chapter 2).

The Registry has been widely used for studies of particular hereditary diseases and congenital malformations[1,3-6,16,18-20,30,45]. Because the Registry is maintained within the vital registration system, it has been possible to arrange for the health surveillance records to be routinely linked with the identifying particulars and relevant statistical information contained in the birth registrations of the individuals. Computerized linkages have also been carried out in the past, with hospital records[33], with the death registrations for the purpose of mortality studies[28], and with the parental marriage records and the birth records of siblings for studies of fertility differentials and of the risks to later born siblings[22,26]. The potential of the Registry has been substantially augmented by these linkage capabilities. Confidentiality of the personal information contained in the records is maintained under the same legal safeguards that are applied to the vital records.

A more detailed description of the Registry appears in Chapter 2.

1. Relevance of the Available Data to Radiation Protection

Over a number of decades, geneticists have urged that exposures of humans to ionizing radiation and other environmental mutagens be restricted so as to avoid as much as possible the induction of mutations leading to cases of hereditary disease in later generations. This general advice has been heeded in virtually all developed countries with regard to exposures to radiation, however there is still much uncertainty concerning the level of safety resulting from a given level of radiation protection[27,29,31,36,38,40-42]. Especially, there is a need to know the magnitude both of the genetic risks and the cancer risks, as it may be vital to consider both in setting standards for safety.

One necessary prerequisite before any increase in genetic load from mutagens can be estimated is baseline information on the collective magnitude of the public health problem from the genetically caused ill health already present in the population[8,9,11,21,35-38,40-42]. The basic load will be composed of a proportion of cases that are due to newly arisen mutations versus those that have been inherited. In disorders where the proportion due to new mutation is high (e.g. 80-90% for achondroplasia) the incidence would be expected to rise more rapidly with a sustained elevation of the mutation rate, than where the ratio is low (e.g. as with Huntington chorea and even more so with the recesssive disorders). It is important to consider another aspect. All genetic discorders occur in a frequency in the

population over the long term that is determined by the rate of recurrent mutation operating against the selection pressures that tend to remove the mutant genes from the gene pool. Dominant conditions would be expected to increase in frequency to a new equilibrium if there were a sustained increase of the mutation rate. The effect of an increase in mutation rate in most of the multifactorial-polygenic conditions such as pyloric stenosis and cleft palate would be expected to be less apparent as several genes are involved for these disorders although there is still debate on the matter. A multifactorial disorder is one where alleles at several gene loci determine vulnerability to express the disorder. The term "multifactorial" will be used in this sense throughout this report.

For the purpose of assessing the present genetic load in the population it is desirable that all cases of hereditary and partially hereditary disease known to the Registry be counted as such, regardless of the presence of non-genetic disorder in the same individual. A particular case may be assigned two or more diagnoses and etiology codes of which only one relates to a genetic condition, and it is important that such cases not be lost from the genetic count. Similarly among the cases of genetic disease as a broad category, there is likely to be a small proportion of individuals who, purely by chance, are affected by two quite independent hereditary conditions. So that this information will not be lost, cross-tabulations are desirable, indicating specifically what genetic diseases and what genetic etiologies occur in the same individuals. For the purpose of estimating the additional numbers of people who might be affected by an artificially induced increase in the mutation rate, it is important not to under-count those categories of genetic disease thought to be most responsive to such a change. Thus, the doubly affected individuals should not be assigned to the category that is the less likely of the two to be responsive to a change in mutation rate.

From the need for this precaution has arisen the concept of a hierarchy of etiologies for the purpose of genetic load estimation. Because DOMINANT diseases are the most likely to respond over a relatively few generations to an elevation of the mutation rate, they are usually viewed as at the top of the hierarchy, followed by the X-LINKED and then RECESSIVE conditions. (Note, however, that in the analysis that follows, Recessive conditions were extracted before the X-linked. This was done to enable more direct comparison with the earlier analysis of this data source by Trimble and Doughty). CHROMOSOMAL anomalies do not rank as high because of uncertainty concerning the shape of the dose-response curve for these at low doses; whereas for point mutations the curve is most likely to be of a linear non-threshold kind, for changes in chromosomal number a non-linear curve seems probable. Thus, induced chromosomal changes may not contribute substantially to the overall genetic risk from radiation and other mutagens unless the exposures are substantial. Finally, MULTIFACTORIAL conditions are at the bottom of the genetic hierarchy because there is even less evidence that they would be affected at

all by a rise in the mutation rate. This hierarchy permits genetically affected *individuals* as distinct from genetic diseases to be counted in a manner compatible with the purposes of radiological risk estimation.

Finally, special mention needs to be made, in the present context, of CONGENITAL ANOMALIES (ICD codes 740-759). This is not an etiological category but a convenient and important grouping of conditions that are quite heterogeneous in their causations. In previous studies the group has been treated as a single entity or only those anomalies with Mendelian patterns of inheritance have been treated separately. However, interest in the group as pertaining to genetic load arises for two reasons. First, it is thought that the group, even after the known Mendelian and chromosomal traits have been separately identified may still contain single gene disorders (e.g. due to new dominant mutation). Secondly, the group is known to contain a substantial number of conditions that are multifactorial in origin. Fortunately, the present records of the Health Surveillance Registry make it possible to identify those cases within the congenital anomaly group thought to be multifactorial in etiology. This is a considerable advance because many earlier studies did not attempt to quantify the relative importance of the multifactorial *versus* the non-genetic categories within the broader "congenital anomalies" grouping.

With the etiological categories defined in the above manner, it should be possible to analyse:

(i) how many of the registered individuals suffer from conditions that are hereditary or partially so,

(ii) how many cases have a single gene etiology (autosomal dominant, autosomal recessive and X linked recessive),

(iii) how many cases have a chromosomal etiology (autosomal and sex chromosome),

(iv) how many individuals are affected by multifactorial traits, (those that are present at birth -"congenital anomalies"- and those that are not).

CHAPTER 2 MATERIALS AND METHOD

2.1. The nature of the data source

(Note: This chapter is based largely on material published by the Health Surveillance Registry, and is reproduced here with the permission of Mr. A.H. Hersom, Director of Vital Statistics, Ministry of Health of British Columbia).

The British Columbia Health Surveillance Registry (HSR) is a programme of the Division of Vital Statistics in the provincial Ministry of Health, and is located in Vancouver. The Registry was established in 1952, following a survey of "Crippling Diseases of Children" carried out in collaboration with Public Health Units. Although original registrations were only of children, since 1961 disabilities occurring at any age have been recorded.

These disabilities are ascertained from a variety of sources. Registrations are received from provincial and metropolitan health departments, certain hospital and rehabilitation centres, and also a number of physicians and other health professionals. In 1964 the sources of ascertainment were extended when death, stillbirth and obstetrical records were included, and again in 1966 when hospital separation records for congenital and other selected conditions in the newborn and children under seven years of age became available. During the ensuing years, additional agencies have agreed to report cases with registerable disabilities, thus substantially increasing the amount of data on file. A list of registering agencies, with the number of cases recorded from each during a recent year (1981) is shown in Appendix 1, Tables A1.1 and 1.2. Further information on the history of the Registry has been published by Lowry et al[17] in 1979 and Baird[2].

By the end of 1984 the HSR master file contained information on 154,071 individuals. Of these, 75,304 had been born in British Columbia between 1952 and 1983 inclusive, and it is from this group of records that the present analysis was performed. Of the remainder there were approximately 6,200 cases born in the 1952-83 period but with a place of birth outside British Columbia, 62,500 cases were born before 1952, 10,000 stillbirths had been registered, and there were a few records of persons in whom place and/or date of birth was not known and could therefore not be used.

In all there are over 60 sources of registration (Appendix 1, Tables A1.1 and 1.2). Currently about 9,000 new cases are reported each year to the Registry from a population of 2,890,000, in which there are now some 40,000 live births annually. Of the more than 100,000 registrants who are still living, about 44 per cent are under

the age of 20. When the Registry was started in 1952 the registrations were only of children, but from 1961 onward disabilities occurring at any age have been recorded.

Cases reported via Death Certificates relate mainly to new cases dying in the neonatal period. In addition to this use of information from Death Certificates, they are used for a routine "death clearance" carried out on the Registry master-file. In this, a quarterly computer linkage (with manual resolution, if needed) is carried out, and date and cause of death is recorded on the case file, but note that the case is retained in the Register.

Spot checks of coding accuracy, and special evaluations for studies such as the present one sometimes uncover errors or ambiguities; however in recent experience these have been few in number.

With an increase in the number of sources of ascertainment there is a potential for counting the same individual twice or more. The possibility of this is likely to be quite low, due to the procedures followed by the Registry staff. These consist of checking each new report against a card index, organized alphabetically by family name, and only creating a new case card if no previous registration has occurred.

Particular care is taken to double-check apparently new registrations of adult females, due to the possibility of a name change following marriage.

Some of the measures taken to reduce the risk of double registration include periodic checks of birth dates vs. diagnoses, an annual check for records with the same birth registration number, and routine scanning of output data for any obvious similarities or discrepancies particularly in cases with similar names (e.g. Mac vs. Mc). Much of this checking is of course done automatically by computer, as is also the routine flagging of incompatible entries such as a date of onset recorded as later than date of death, as well as improbable or impossible combinations of diagnostic and etiology codes.

Investigation of questionable cases is greatly facilitated by the fact that, as part of the Division of Vital Statistics, the Registry has ready access to the Provincial records of Births, Marriages and Deaths, so that family links may be identified.

Over the years, the format of the case-record has changed. An early example is shown in Appendix 1, Table A1.3. The records of some individuals include follow-up information, often concerning level of disability, development of signs or symptoms of new diagnoses.

In 1974 the system was computerized, using the code-sheet shown in Appendix 1, Table A1.4. Four diagnoses could be accommodated, etiology code for the first two

diagnoses, and the McKusick number (where applicable) to the first diagnosis or death.

In 1983 major changes occurred in the entire process:

(i) The new record card (Appendix 1, Table A1.5) now served also as the data entry form, and data entry was from now on performed by Registry staff, rather than by batch processing at a remote site. This had the important side-effect of improving the quality of data entry, since ambiguities or errors were more likely to be identified and resolved on the spot, by personnel familiar with the terminology and purpose of the data.

(ii) Room was provided both on the record card and in the computer programme for 15 (expandable up to 20) diagnoses per case each of which could potentially have its own etiology code and McKusick number. Space is also provided for a "functional level" to be ascribed to each diagnosis. This capability has not yet been exploited, mainly because of the difficulty in arriving at a simple, uniform system of coding -- plus the problem that functional level(s) may well change over the years.

(iii) If and when an additional diagnosis needed to be added to a record, under the pre-1983 system it might be necessary to re-arrange the previous diagnoses so that the most important (in the sense of affecting the well-being of the individual) would have one of the two available etiology codes and (possibly) the one available McKusick number. Since 1983 a new diagnosis is simply added to the list, without any re-arrangement of the previous diagnoses. An important corollary of this is that the date of diagnosis or notification is now available for each diagnosis. Previously only one date was available -- when the case was first notified, or the first known date of onset or diagnosis.

(iv) The computer programme can now accept up to 5- digit ICD numbers. A few of these (e.g. diabetes) are prescribed in the 9th revision of the ICD, but in addition the Registry may use a 5th digit to provide more detailed information for the purpose of special studies and has a number of special Registry codes to more accurately classify disorders.

(v) Some additional points on the new system are that retrieval and analysis of data is much more rapid now that the computer processing is entirely in-house. Also, although the new system was only introduced in the final year of the present study period (1952 - 1983), many older case-records have been updated and expanded as new information arrived and cards were "pulled".

The etiology codes used by the Registry are shown in Appendix 1,Table A1.6.

In 1979 the diagnostic codes were converted manually and by computer to ICD 9 from ICD 8 under the direction of the late Helen Colls[10]. In addition as noted above some "special" ICD 9 codes have been used by the Registry, and some regular ICD 9 codes have been used with a different meaning by the Registry (Appendix 1, Table A1.7). In the detailed tabulations of this report, such codes have been identified by an asterisk.

The current recording instructions and format may also be found in Appendix 1, Tables A1.8-1.9. Approximately 90% of the diagnostic codes, etiologies, and McKusick numbers are entered by Registry staff, the other 10% have been entered after review by the medical and genetic consultants (initially Dr J.R. Miller, followed by RBL, then PAB).

2. Processing of the Data

An overall summary of the data available is presented in Table 2.1.

So that this report can be compared with the report published by Trimble and Doughty[36] in 1974 on Registry data, the major differences in methodology between the two are outlined below:

(i) Since data from a greater number of years were available to us, we have been able to divide the records into three time periods that are each 10 or more years in length (1952-63, 64-73, 74-83) this has meant that for each category of disorder we have been able to choose the "decade" which seemed likely to reflect most closely the genetic load for that disorder in the population. Thus each of our rates is based on at least 10 years data, compared to the 3-year periods used by Trimble and Doughty (1964-6 for hereditary diseases, and 1967-9 for congenital malformations).

(ii) The choice of "best" decade has been done for each individual diagnosis within each etiological group as well as by the grouping into Dominant, Recessive, etc.

(iii) Although we have in general followed the same hierarchical approach as Trimble and Doughty, we chose not to move from single-gene and chromosome disorders to "Congenital Anomalies" then "other Multifactorial". Rather, multifactorial disorders have been identified separately, and examined after chromosome disorders in the hierarchy. Rather than count all the many diagnoses that might possibly have some multifactorial component, we have restricted ourselves to those relatively common conditions that are generally accepted as having a major multifactorial component. Detailed data are provided, so that the reader may make amendments if so desired.

(iv) Data on all congenital anomalies are also presented so that the data can be compared to other studies.

(v) We have not made any "adjustments" to rates to compensate for under-ascertainment, out-migration, etc, as was done by Trimble and Doughty[36]. The reason for this is that (a) a there is little or no hard evidence on which to base these adjustments, and (b) if the rates are to be used as a baseline against which to determine whether changes are occurring in the frequency of certain disorders, then the increase (or decrease) is likely to be affected by similar distortions, and the relative change should therefore be unaffected.

(vi) As explained in the previous chapter, until 1983 the computer programme could accept etiological diagnoses for only 2 of the 4 diagnoses that could be listed for each case. Trimble and Doughty's analysis therefore ignored the 3rd and 4th diagnoses on the case-record. It should be clearly understood, that although the expanded record capability was only introduced in 1983, there are a substantial number of records that although started before 1983 have subsequently been "pulled" from the files for one reason or another, and at that time they are converted to the new format. This expansion of possible diagnoses is unlikely to have had a major effect on frequencies.

3. Procedure

Arising out of the capability of assigning an etiology to each ICD9 code is the question of whether -- given two "competing" diagnoses with the same etiological classification – which diagnosis should be given priority? This question is not an easy one to answer, since although the initial and "obvious" solution would appear to be to assign the case to the most clinically significant diagnosis this creates several other problems. For example many cases have little or no information on the degree of disability caused by each diagnosis, and even where it is recorded on the written case card it is not coded to the computer record. Assigning priorities for diagnosis would therefore have involved a great deal of manual checking of files, and even then would have been incomplete. Another problem is that the relative importance of diagnoses might change -- for example in a given case a life-threatening cardiac condition might be clearly the most important diagnosis until age 5, at which time surgical correction of the heart defect leaves mental retardation as the most important condition. Alternatively, two conditions may be equally important clinically.

Although this initially appeared to be a major obstacle in the analysis, it was in fact found to be relatively easy to manage. Any remaining ambiguities had a very small impact on the overall rate for a condition. The process is illustrated in Chapter

3, dealing with the highest-ranked of the single-gene conditions, the Dominant disorders.

In subsequent chapters the examination of disorders by etiologic category is initially carried out in the same order as that used by Trimble and Doughty[36]. Dominant, Recessive, X-Linked, Autosomal chromosome, Sex chromosome. However, at this point we chose to use a different ranking process, and examined Multifactorial cases, rather than Congenital Anomalies, since the latter are not an etiologic category.

To help avoid possible confusion between rates (per million) and absolute numbers of cases, all rates are given to one decimal place.

TABLE 2.1

Summary table of total live births, registered cases, and rates per million live births in British Columbia, by three birth periods

	1952-63		1964-73		1974-83		Total 1952-83	
	N	Rate	N	Rate	N	Rate	N	Rate
Live Births	437503		344665		387705		1169873	
All registered cases	19476	44516.3	25909	75171.5	29919	77169.5	75304	64369.4
Cases with single diagnosis only	13123 [67%]	29995.2	19746 [76%]	57290.4	21639 [72%]	55813.1	54508 [72%]	46593.1
cases with 2 or more diagnoses	6353 [33%]	14521.0	6163 [24%]	17881.1	8280 [28%]	21356.4	20796 [28%]	17776.3

CHAPTER 3 SINGLE GENE DISORDERS

1. Autosomal Dominant

The first "culling" of the data set extracted all those cases in which any diagnosis had an '02' (Dominant) etiology following an ICD diagnosis code number. In cases with more than one diagnosis, the relative position of the dominant diagnosis (i.e. first, second, third, etc) was ignored.

Cases with only a single '02' diagnosis (with or without additional diagnoses of lower rank) accounted for almost 75% of the 1041 Dominant cases identified. However, there were 280 cases in which there was more than one diagnosis with an 02 etiology code. These cases were grouped (by H.B.N.) according to the McKusick number where this was present on the file, and a single most appropriate ICD number was suggested. This suggestion was then either approved or changed by consensus of the two medical genetic consultants (PAB, RBL). To illustrate this process, Appendix 2 contains a copy of the first page of this set of worksheets, as well as a copy of one page of the raw data from which it was created. (Table A2.1).

This process reduced the number of ambiguous cases to 36, in which no McKusick number was present on the file. The most appropriate classification of these 36 cases was then decided by consultation between HBN, PAB, and RBL.

In this way a final summary tabulation could be prepared in which the dominant cases were classified by a single ICD diagnosis and by three birth-year periods. Rates per million live births were calculated for each diagnosis within each of the three periods (Table 3.1, and Appendix 2, Table A2.2), the most appropriate of the three rates for each diagnosis was chosen. This was usually the highest, on the assumption that under- rather than over-ascertainment is the most likely source of error, particularly in conditions that are late in appearing.

This process resulted in an overall rate of 1395 per million live births.

The low rate for the third period almost certainly reflects the typically late onset of disability in dominant disorders. The fact that the rate for the oldest cohort (1952-63 births) is substantially lower than the middle cohort (1964-73 births) probably reflects the increased completeness of ascertainment in more recent years.

It may be noted that the figure of 1395 per million is some 39% higher than the overall figure of 1004 per million for the highest (middle) birth cohort, and 57% higher than the overall figure of 890 per million for all 32 years (Table 3.1).

The previous analysis of this data set by Trimble and Doughty found 61 cases with dominant disorders among the 103,980 live births that occurred in the years 1964-67. This gave an exact rate of 586.7 per million live births, a figure that was rounded to .06% for a "minimal" estimate and then increased to .08% for an "adjusted" rate, to take into account possible underascertainment due to delay in disease onset, migration, and incompleteness of ascertainment.

2. Autosomal Recessive

After the dominants had been removed all cases with a Registry etiology of '03' were listed. These totalled 1181.

Compared to the Dominant disorders, there were relatively few ambiguous cases, and these were dealt with by the same procedure previously outlined for Dominants.

A summary of the final tabulation is shown in Table 3.2, and the complete figures in Appendix 2, Table A2.3.

The overall rate was 1008 per million, with the middle cohort again showing the highest rate, at 1178 per million. When the highest rate for each individual diagnosis were summed, the rate was 1655 per million. This final figure is 40% higher than the "crude" rate for the middle cohort, and 64% higher than the overall rate for the 32 year period.

The previous rate for Recessives found by Trimble and Doughty[36] was 904.0 p.m.l.b. (94 cases in 103,980), rounded to .090% for a "minimal" estimate, and increased to .11% for the final "adjusted" figure.

3. X-Linked Disorders

Due in part to the relatively small number of cases in this category (Registry etiology 04), there were few ambiguities, and these were quickly resolved.

The 394 cases gave an overall rate of 337 per million, with a high 'crude' rate of 383 per million in the second period, and a "detailed" overall maximum rate of 532 per million live births (Table 3.3, and Appendix Table A3.4) .

Trimble and Doughty's earlier analysis of this data set[36] had found a rate of 298.1 p.m.l.b., (31 cases in 103,980 live births) for a minimal estimate of .03%, increased to .04% as a final "adjusted" rate.

Table 3.1

Frequencies of the most common dominant disorders. (For a complete listing, see Appendix 2, Table A 2.2)
*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD9	DOMINANT CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
190.5	Retina, Malignant Neoplasm	6	13.7	14	40.6	16	41.3	36	30.8
237.7	Neurofibromatosis	34	77.7	33	95.7	32	82.5	99	84.6
277.8	Other Disorders of Metabolism	1	2.3	7	20.3	11	28.4	19	16.2
282.0	Hereditary Spherocytosis	12	27.4	18	52.2	20	51.6	50	42.7
286.4	Von Willebrand's Disease	5	11.4	7	20.3	8	20.6	20	17.1
359.2	Myotonic Disorders	14	32.0	8	23.2	6	15.5	28	23.9
362.7	Hereditary Retinal Dystrophies	13	29.7	0	0.0	0	0.0	13	11.1
379.5	Nystagmus and Other Irregular Eye Movements	14	32.0	2	5.8	3	7.7	19	16.2
389.1	Sensorineural Deafness	3	6.9	15	43.5	4	10.3	22	18.8
743.3	Congenital Cataract and Lens Anomalies	21	48.0	10	29.0	5	12.9	36	30.8
755.0	Polydactyly	6	13.7	16	46.4	14	36.1	36	30.8
755.5*	Other Anom of Upper Limb, Inc Shoulder Girdle	3	6.9	2	5.8	9	23.2	14	12.0
756.0*	Anomalies of Skull and Face Bones	9	20.6	11	31.9	14	36.1	34	29.1
756.4	Chondrodystrophy	48	109.7	21	60.9	20	51.6	89	76.1
756.5	Osteodystrophies	24	54.9	31	89.9	29	74.8	84	71.8
756.8	Other Spec Anom of Muscle, Tendon, Fascia, etc.	13	29.7	14	40.6	7	18.1	34	29.1
756.9	Unspec Anom of Musculoskeletal System	2	4.6	8	23.2	0	0.0	10	8.5
757.3*	Other Specified Congenital Anomalies of Skin	11	25.1	5	14.5	6	15.5	22	18.8
759.5	Tuberous Sclerosis	13	29.7	23	66.7	22	56.7	58	49.6
759.8	Other Specified Congenital Anomalies	17	38.9	16	46.4	9	23.2	42	35.9
	All Other Dominant Conditions	110	251.4	85	246.6	81	208.9	276	235.9
TOTAL		379	866.3	346	1003.9	316	815.1	1041	889.8
SUM OF HIGHEST INDIVIDUAL RATES									1395.4

Table 3.2

Frequencies of the most common recessive disorders. (For a complete listing, see Appendix 2, Table A 2.3)
*Indicates special Registry Code (see Appendix 1, Table A1.7)

ICD9	RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
255.1	Hyperaldosteronism	13	29.7	7	20.3	1	2.6	21	18.0
255.2	Adrenogenital Disorders	5	11.4	8	23.2	12	31.0	25	21.4
270.1	Phenylketonuria	26	59.4	18	52.2	31	80.0	75	64.1
270.2*	Other Disturbances of Aromatic Amino-Acid Metab	22	50.3	19	55.1	16	41.3	57	48.7
271.0	Glycogenosis	3	6.9	12	34.8	8	20.6	23	19.7
272.7	Lipidoses	4	9.1	10	29.0	4	10.3	18	15.4
277.0	Cystic Fibrosis	80	182.9	105	304.6	87	224.4	272	232.5
277.5	Mucopolysaccharidosis	8	18.3	11	31.9	2	5.2	21	18.0
279.0	Deficiency of Humoral Immunity	4	9.1	12	34.8	4	10.3	20	17.1
282.4	Thalassaemias	15	34.3	7	20.3	16	41.3	38	32.5
330.1	Cerebral Lipidoses	5	11.4	10	29.0	3	7.7	18	15.4
335.0	Werdnig-Hoffmann Disease	6	13.7	19	55.1	15	38.7	40	34.2
358.8*	Other Myoneural Disorders	18	41.1	4	11.6	0	0.0	22	18.8
359.1	Hereditary Progressive Muscular Dystrophy	19	43.4	3	8.7	0	0.0	22	18.8
362.7	Hereditary Retinal Dystrophies	21	48.0	10	29.0	0	0.0	31	26.5
389.1	Sensorineural Deafness	9	20.6	12	34.8	8	20.6	29	24.8
389.9*	Unspecified Deafness	20	45.7	12	34.8	4	10.3	36	30.8
753.1	Cystic Kidney Disease	11	25.1	10	29.0	7	18.1	28	23.9
756.5	Osteodystrophies	1	2.3	8	23.2	7	18.1	16	13.7
759.8	Other Specified Anomalies	7	16.0	18	52.2	21	54.2	46	39.3
	All Other Recessive Conditions	104	237.7	91	264.0	126	325.0	321	274.4
TOTAL		401	916.6	406	1178.0	372	959.5	1179	1007.8
SUM OF HIGHEST INDIVIDUAL RATES									1655.3

Table 3.3

Frequencies of the most common X-linked disorders. (For complete listing, see Appendix 2, Table A 2.4)
*Indicates special Registry code (see Appendix 1, Table A1.7)

X-LINKED CONDITIONS		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9		N	Rate	N	Rate	N	Rate	N	Rate
257.8	Other Testicular Dysfunction	8	18.3	0	0.0	7	18.1	15	12.8
270.6	Disorders of Urea Cycle Metabolism	1	2.3	0	0.0	3	7.7	4	3.4
275.4	Disorders of Calcium Metabolism	0	0.0	2	5.8	0	0.0	2	1.7
277.5	Mucopolysaccharidosis	3	6.9	3	8.7	0	0.0	6	5.1
279.0	Deficiency of Humoral Immunity	6	13.7	2	5.8	0	0.0	8	6.8
282.2	Anaemia Due to Dis of Gluthathione Metab	3	6.9	2	5.8	14	36.1	19	16.2
286.0	Congenital Factor VIII Disorder	28	64.0	24	69.6	14	36.1	66	56.4
286.1	Congenital Factor IX Disorder	7	16.0	10	29.0	1	2.6	18	15.4
288.1	Functional Dis of Neutrophil Polymorphs	0	0.0	0	0.0	3	7.7	3	2.6
317.2*	Mild Mental Retardation	3	6.9	1	2.9	0	0.0	4	3.4
318.0	Moderate Mental Retardation	4	9.1	1	2.9	0	0.0	5	4.3
318.2	Profound Mental Retardation	1	2.3	2	5.8	0	0.0	3	2.6
319	Unspecified Mental Retardation	1	2.3	1	2.9	4	10.3	6	5.1
359.1	Hereditary Progressive Muscular Dystrophy	43	98.3	34	98.6	13	33.5	90	76.9
368.5	Colour Vision Deficiencies	29	66.3	32	92.8	14	36.1	75	64.1
588.1	Nephrogenic Diabetes Insipidus	3	6.9	2	5.8	4	10.3	9	7.7
743.5	Congenital Anomalies of Posterior Segment	2	4.6	2	5.8	3	7.7	7	6.0
756.0*	Anomalies of Skull and Face Bones	2	4.6	1	2.9	3	7.7	6	5.1
757.3*	Other Specified Anomalies of Skin	3	6.9	3	8.7	7	18.1	13	11.1
759.8	Other Specified Congenital Anomalies	1	2.3	0	0.0	3	7.7	4	3.4
	All Other X-linked Conditions	9	20.6	10	29.0	12	31.0	31	26.5
TOTAL		157	358.9	132	383.0	105	270.8	394	336.8
SUM OF HIGHEST INDIVIDUAL RATES									532.4

CHAPTER 4 CHROMOSOME DISORDERS

1. Autosomal Chromosome Disorders

As with previous single-gene disorders, the initial step was to list all those cases with ICD codes 758.0 to 758.9 and/or etiology code of 05. Review of a few cases with ambiguous or multiple 05 etiologies resulted in the classification shown in Table 4.1.

There were 1664 cases registered for an overall rate of 1422.4 cases per million live-births. It should be noted that a small number of balanced translocations in clinically normal individuals have been included. The "crude" rate was 1364.6 per million in the first period, 1534.8 in the second, and 1387.7 in the third, with a maximum detailed rate of 1718.3 per million live-births.

Trimble and Doughty's estimate was 0.157%, (1567.6 p.m.l.b., based on 163 cases in 103,980 live births), "adjusted" to a final estimate of .20%, or 2000 p.m.l.b[36].

The rates for chromosome anomalies observed by surveys from the literature[12,14] are higher than those observed by the Registry. This is to be expected since under-ascertainment is likely for many cases of less obvious chromosome anomalies such as deletions and for individuals dying prior to testing. The rates published refer to consecutive series of individuals tested and can be expected to be higher than those recorded in the Registry.

2. Sex Chromosome Disorders

Sex chromosome disorders (Registry etiology code 06) were the smallest group of cases in the hierarchy, with a total of 136 cases registered over the 32 year period. The correspondingly few ambiguities were quickly resolved, resulting in the numbers and rates shown in Table 4.2.

Compared to the crude overall rate of 116.3 per million live births, the first period showed a rate of 146.3 per million, while the detailed summation of individual rates resulted in a maximum estimate of 152.3 per million live births.

The corresponding figure obtained by Trimble and Doughty was 48.1 per million live births (5 cases in 103,980 births), rounded off without adjustment to .005%.

Table 4.1

Frequencies of autosomal chromosome conditions (complete list)

AUTOSOMAL CHROMOSOME		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9		N	Rate	N	Rate	N	Rate	N	Rate
758.0	Down Syndrome	571	1305.1	460	1334.6	394	1016.2	1425	1218.1
758.1	Patau Syndrome (Trisomy 13)	3	6.9	15	43.5	22	56.7	40	34.2
758.2	Edward Syndrome (Trisomy 18)	1	2.3	31	89.9	57	147.0	89	76.1
758.3	Autosomal Deletion Syndromes	4	9.1	4	11.6	26	67.1	34	29.1
758.4	Balanced Autosomal Translocation in Normal	11	25.1	5	14.5	5	12.9	21	18.0
758.5	Other Conditions Due to Autosomal Anomalies	6	13.7	14	40.6	31	80.0	51	43.6
758.9	Anomaly of Unspecified Chromosome	1	2.3	0	0.0	3	7.7	4	3.4
TOTAL		597	1364.6	529	1534.8	538	1387.7	1664	1422.4
SUM OF HIGHEST INDIVIDUAL RATES									1718.3

Table 4.2

Frequencies of sex chromosomal conditions (complete list)

SEX CHROMOSOMAL CONDITIONS		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9		N	Rate	N	Rate	N	Rate	N	Rate
758.6	Gonadal Dysgenesis	33	75.4	26	75.4	23	59.3	82	70.1
758.7	Klinefelter Syndrome	28	64.0	11	31.9	5	12.9	44	37.6
758.8	Other Sex Chromosome Anomalies	3	6.9	2	5.8	5	12.9	10	8.5
TOTAL		64	146.3	39	113.2	33	85.1	136	116.3
SUM OF HIGHEST INDIVIDUAL RATES									152.3

CHAPTER 5 MULTIFACTORIAL DISORDERS

5.1 As pointed out in "Methods" a difference in this analysis compared to others, including the previous Trimble and Doughty study of the B.C. Registry data, is that after ranking single-gene and chromosome disorders, we did not then examine "Congenital Malformations of Multifactorial origin", *followed* by "Other Multifactorial". Rather, we avoided using Congenital Malformations in the ranking process at all, since it is -- unlike the other categories -- not an etiological classification. Thus we moved directly from sex-linked disorders to examine the frequency of selected multifactorial disorders.

The procedure adopted was that the two medical geneticists (PAB and RBL) identified 22 diagnoses which they felt were generally agreed to have a major multifactorial genetic component. Cases with at least one of these diagnoses were then identified from those cases remaining after the removal of the previously described hierarchy of Dominant through Sex-linked disorders. However, cases with no ICD code in this list were <u>not</u> included if the associated Registry etiological code indicated a cause that was non-genetic - e.g. pre-natal infection, birth trauma, etc. The Registry codes accepted were: 00, 07, 21, 66, 71, and 75 (see Appendix 1 Table A1.6). In addition, strabismus cases with an 01 etiology code ("Genetic-unspecified") were included.

Various methods were explored to deal with the problem of cases having multiple diagnoses. It was found that the most effective way of handling this problem was to first count for each diagnosis of interest the cases with only one diagnosis (Table 5.1) and choose the most appropriate birth period, to give the "minimum estimate". Cases with more than one diagnosis were then grouped according to the second (or more) diagnosis, and the medical geneticists decided which, if any, should be accepted. Combining the two sets of figures yielded "expanded minimum" estimates (Table 5.2). The cases added were those where the other code(s) indicated a disorder likely to be a consequence of the initial multifactorial condition. These are listed later in this section.

Thus the individuals counted in Table 5.2 have either one disorder only, or disorders which, although coded to different ICD9 codes, are indeed basically the consequence of one condition. An example would be an individual with cleft lip and palate who also had malocclusion. Included in this table are some conditions, such as schizophrenia, idiopathic scoliosis, dislocatable hip, whose multifactorial etiology is controversial. This is done since there is evidence that they may be multifactorial, and they have been listed separately so that if the reader wishes, they may be omitted. There are several other common disorders that have not been included, such as alcoholism, or the neuroses, which undoubtedly have an

important genetic component, but whether in fact the actual basis is multifactorial, is not clear.

The number of individuals counted in this way is a conservative estimate of the proportion of the population with multifactorially-determined disease. This is because individuals who have additional unrelated disabilities of any kind have not been included. It would not have been practical to evaluate on an individual basis the large number of individuals who had a possibly multifactorially caused condition, occurring with other disabilities as well, to see if appropriate to allocate to the multifactorial category. Thus those individuals with additional disabilities are arbitrarily not assigned to the multifactorial group.

All cases on the Registry where a specific etiology code had been assigned to a condition which might otherwise have been interpreted as multifactorial have been omitted from the table. For example, if there was a known genetic etiology or a known environmental cause, conditions such as congenital heart disease, or cleft lip and palate, have of course not been included in the table.

It is necessary to make a few explanatory comments about some of the conditions. With regard to congenital dislocated hip, and congenital dislocatable hip, the Registry has coded these cases to 754.3 and 754.9 respectively. The latter is not a standard ICD9 code but a special use by the Registry (see Table A1.7). Since it is likely that the "dislocatable" category may also have a multifactorial etiology, these have been included in the table. The Registry also has a special interpretation of the club foot category. Cases normally coded in ICD9 to 754.5, 754.6, and 754.7 are all coded to 754.7. This then is felt to reflect the number of individuals with club foot of different kinds.

Since malocclusion is such a common concomitant of cleft lip and palate, it was felt justified to treat individuals with both these disorders as still having a multifactorially determined condition and they have been included in the "expanded minimum" estimate (Table 5.2). Similarly, in the category of congenital heart disease, even if more than one heart malformation was present, it was still felt appropriate to assign them to the category of multifactorial provided they had no additional malformations coded outside this heart malformation section. Individuals with asthma or atopic eczema likely have the same general allergic diathesis, and thus individuals having both or either condition are included in the table.

Approximately 25% of the patients with Hirschsprung's Disease had non-regional anomalies and thus have been omitted from consideration in the total of cases of Hirschsprung of multifactorial etiology. Although a further 7% of cases of Hirschsprung's Disease had local regional anomalies, it was felt that these had

occurred secondarily to the local bowel dilatation. Thus, those cases with associated regional anomalies have been included in the count of those individuals with multifactorial conditions[34].

In a recent study, the incidence of isolated Hypospadias in the province during 1966-1981 was found to be 3.55 per 1,000 live born male infants[15]. Unlike this analysis the cases with additional anomalies were included. but the main reason for the much lower rate (1.8 per 1000) found in this study is, of course, that in the present analysis we are using total live births as the denominator, rather than male births only.

Since retardation of some degree is a frequent complication of hydrocephalus, cases of hydrocephalus have still been accepted as multifactorial if retardation is present as well. Since premature birth may be a causative factor of intracranial bleeding and consequent hydrocephalus, those cases where prematurity was present have been omitted from the table, as being better not treated as multifactorial in etiology.

It was decided that it was appropriate to treat those cases of borderline or mild mental retardation with no other malformations or disorders as multifactorial in etiology. In Appendix 4 the frequency of all cases of mental retardation listed in the Registry is examined since of course it is quite possible that a proportion of cases assigned to the "moderate" category or the "unspecified" category should also appropriately be added to the multifactorial table. However, what this proportion is is difficult to estimate and it is felt that the conservative approach of not including these in multifactorial is more appropriate.

Diabetes mellitus is also a very difficult category to rigorously assign. Any cases associated with known specific cause, for example such as diabetes mellitus occurring in Klinefelter Syndrome, have been omitted from the table. It is recognized that this is a heterogeneous group, in that juvenile onset and adult onset are likely to have different genetic components to their etiology. However, it is felt that in our present state of knowledge where the majority of cases of diabetes mellitus of unknown cause are likely to have a genetic component, that they should be included in this table of multifactorial conditions. Further, none of the cases in this study would be more than 32 years old by the end of 1983.

It will be noted that hypertension, although viewed by many as having a multifactorial etiology, is not included in the table. This is because we would be unlikely to ascertain cases of individuals who had only hypertension and no complications. Thus with known seriously inadequate ascertainment, it seemed better to omit this condition from the table.

Epilepsy is also a difficult category to interpret in that even in cases without a known cause, it is likely that heterogeneity exists. However, since there is undoubtedly a genetic component to this disorder, it was felt appropriate to include this group in the "multifactorial" load.

Details of the individual diagnostic categories follow: -

1. Diabetes Mellitus (ICD 250)
   Period of choice: 1952-63
   Cases with single diagnosis: 526
   Minimum estimate of rate: 1202.3 per million live births
   Cases accepted with 2 or more diagnoses: 37
   Second (or more) diagnoses present in the 37 additional cases:
   ICD 307, 308, 309, 312, 313, 357.2, 362.0, 366.4, 369, 401.9
   Expanded minimum 563 cases; rate 1286.8 p.m.l.b.

2. Schizophrenic Psychoses (ICD 295)
   Period of choice: 1952-63
   Cases with single diagnoses: 181
   Minimum estimate of rate: 413.7 per million live births
   Cases accepted with 2 or more diagnoses: 13
   Second (or more) diagnoses present in the 13 additional cases:-
   ICD 296.6, 300.1, 300.4, 301.6/7, 309.9, 311.
   Expanded minimum 194 cases; rate 443.4 p.m.l.b.

3. Affective Psychoses (ICD 296) (mainly manic-depressive)
   Period of choice: 1952-63
   Cases with single diagnosis: 10
   Minimum estimate of rate: 22.9 per million live births
   Cases with 2 or more diagnoses: 3
   Second (or more) diagnoses present in the 3 additional cases: -
   ICD 302.6, 251.2 (with 301.6), and 301.8 (with 301.7)
   Expanded minimum 13 cases; rate 29.7 p.m.l.b.

4. Borderline Mental Retardation (ICD 317.1)
   (Note: 317.1 is a Registry modification of the ICD
   classification ICD 317 "Mild Mental Retardation" -Table A1.7)
   Period of choice: 1952-63
   Cases with single diagnosis: 314
   Minimum estimate of rate: 717.7 per million live births
   Cases accepted with 2 or more diagnoses: 98
   Second (or more) diagnoses present in the 98 additional cases: -
   ICD 259.4, 301, 307.0, 309, 312, 313, 315, 781.3, 783.4.
   Expanded minimum 412 cases; rate 941.7 p.m.l.b

5. Mild Mental Retardation (ICD 317.2)
(Note: 317.2 is a Registry modification of the ICD classification ICD 317 "Mild Mental Retardation" - Table A1.7)
Period of choice: 1952-63
Cases with single diagnosis: 181
Minimum estimate of rate: 413.7 per million live births
Cases accepted with 2 or more diagnoses: 78
Second (or more) diagnoses in the 78 additional cases: -
ICD 295.1/6/9, 299.9, 301, 302.9, 309.9, 312, 313, 315, 783.4, 784.5
Expanded minimum 259 cases; rate 592.0 p.m.l.b.

6. Epilepsy (ICD 345.0-.5, .7-.9) (345.6 "Infantile Spasms" has been omitted).
Period of choice: 1952-63
Cases with single diagnosis: 807
Minimum estimate of rate: 1844.6 per million live births
Cases accepted with 2 or more diagnoses: 39
Second (or more) diagnoses present in the 39 additional cases:
ICD 300 - 316
Expanded minimum 846 cases; rate 1933.7p.m.l.b.

7. Strabismus (ICD 378)
(Note: 378 is a special Registry code - see Table A1.7)
Period of choice: 1964-73
Cases with single diagnosis: 3566
Minimum estimate of rate: 10346.3 per million live births
Cases accepted with 2 or more diagnoses: 27
Second (or more) diagnoses present in the 27 additional cases: -
ICD 368.0, 369.1/6/7/9.
Expanded minimum 3593 cases; rate 10424.6 p.m.l.b.

8. Asthma (ICD 493)
Period of choice: 1952-63
Cases with single diagnosis: 124
Minimum estimate of rate: 283.4 per million live births
Cases accepted with 2 or more diagnoses: 27
Second (or more) diagnoses present in the 27 additional cases: -
ICD 301 - 313, 316, 367.0- .2, 490, 491.9, 492, 494, 692.9
Expanded minimum 151 cases: rate 345.1 p.m.l.b

9. Inguinal Hernia (ICD 550)
Period of choice: 1974-83
Cases with single diagnosis: 1997
Minimum estimate of rate: 5150.8 per million live births
Cases accepted with 2 or more diagnoses: 394
Second (or more) diagnoses present in the 394 additional cases: -
ICD 301 - 313, 316, 367.0- .2, 490, 491.9, 492, 494, 692.9
Expanded minimum 2391 cases; rate 6167.1 p.m.l.b.

10. Eczema (ICD 691.8)
Period of choice: 1952-63
Cases with single diagnosis: 37
Minimum estimate of rate: 84.6 per million live birth
Cases accepted with 2 or more diagnoses: 0
Expanded minimum 37 cases; rate 84.6 p.m.l.b.

11. Anencephaly (ICD 740)
Period of choice: 1974-83
Cases with single diagnosis: 50
Minimum estimate of rate: 129.0 per million live births
Cases accepted with 2 or more diagnoses:
Second (or more) diagnoses present in the 9 additional cases: -
ICD 765.1, 769
Expanded minimum 59 cases; rate 152.2 p.m.l.b.

12. Spina Bifida (ICD 741)
Period of choice: 1974-83 (chosen to be congruent with Anencephaly)
Cases with single diagnosis: 67
Minimum estimate of rate: 172.8 per million live births
Cases accepted with 2 or more diagnoses: 11
Second (or more) diagnoses present in the 11 additional cases: -
ICD 344.0-5, 344.6, 685.1, 756.1
Expanded minimum 78 cases; rate 201.2 p.m.l.b.

13. Encephalocele (ICD 742.0)
Period of choice: 1974-83 (chosen to be congruent with other related neural tube problems)
Cases with single diagnoses: 8
Minimum estimate of rate: 20.6 per million live birth
Cases accepted with 2 or more diagnoses: 2
Second (or more) diagnoses present in the 2 additional cases: - ICD 756.1, 765.1
Expanded minimum 10 cases; rate 25.8 p.m.l.b.

14. Congenital Hydrocephalus (ICD 742.3)
Period of choice: 1964-73
Cases with single diagnosis: 99
Minimum estimate of rate: 287.2 per million live births
Cases accepted with 2 or more diagnoses: 25
Second (or more) diagnoses present in the 25 additional cases: - ICD 315, 317.1/2, 319, 343, 345.0- .5, 345.7- .9, 742.0, 783.4, 784.4
Expanded minimum 124 cases; rate 359.8p.m.l.b.

15. Congenital Anomalies of Heart and Circulatory System (ICD 745-7)
Period of choice: 1964-73
Cases with single diagnosis: 1699
Minimum estimate of rate: 4929.4 per million live births
Cases accepted with 2 or more diagnoses: 30
Second (or more) diagnoses present in the 30 additional cases: ICD 300-316, 416, 424.1, 428, 430, 434.1, 765.1, 769, 770
Expanded minimum 1729 cases; rate 5016.5 p.m.l.b.

16. Cleft Palate and Lip (ICD 749)
Period of choice: 1964-73
Cases with single diagnosis: 445
Minimum estimate of rate: 1291.1 per million live births
Cases accepted with 2 or more diagnoses: 45
Second (or more) diagnoses present in the 45 additional cases: - ICD 389.0/9, 524.0, 750.2, 784.5
Expanded minimum 490 cases; rate 1421.7 p.m.l.b.
For interest, figures for cleft palate alone (ICD 749.0) were separated out. There were 139 cases with this as the only diagnosis, and a further 31 cases accepted, for a total of 170, and a rate of 493.2 p.m.l.b.

17. Congenital Hypertrophic Pyloric Stenosis (ICD 750.5)
Period of choice: 1974-83
Cases with single diagnosis: 909
Minimum estimate of rate: 2344.6 per million live birth
Cases accepted with 2 or more diagnoses: 8
Second (or more) diagnoses present in the 8 additional cases: -
ICD 283.9, 530.1, 765, 769
Expanded minimum 917 cases; rate 2365.2 p.m.l.b.

18. Hirschsprung's Disease and Other Congenital Functional Disorders of Colon (ICD 751.3)
Period of choice: 1964-73
Cases with single diagnosis: 60
Minimum estimate of rate: 174.1 per million live births
Cases accepted with 2 or more diagnoses: 4
Second (or more) diagnoses present in the 4 additional cases: -
ICD 751.2, 753.2, 765.1
Expanded minimum 64 cases; rate 185.7 p.m.l.b.

19. Hypospadias and Epispadias (ICD 752.6)
Period of choice: 1964-73
Cases with single diagnosis: 558
Minimum estimate of rate: 1619.0 per million live births
Cases accepted with 2 or more diagnoses: 70
Second (or more) diagnoses present in the 70 additional cases: -
ICD 598.8, 598.9, 599.1, 753.6/8
Expanded minimum 628 cases; rate 1822.1 p.m.l.b.

20. Clubfoot ("Other Deformities of Feet" ICD 754.7) (See Table A1.7)
Period of choice: 1974-83
Cases with single diagnosis: 1967
Minimum estimate of rate: 5073.4 per million live births
Cases accepted with 2 or more diagnoses: 16
Second (or more) diagnoses present in the 16 additional cases:
ICD 767.5, 769, 770.
Expanded minimum 1983 cases; rate 5114.7 p.m.l.b.

21. Congenital Dislocation of Hip (ICD 754.3)
Period of choice: 1974-83
Cases with single diagnosis: 1322
Minimum estimate of rate: 3409.8 per million live births
Cases with 2 or more diagnoses: 11
Second (or more) diagnoses present in the 11 additional cases: -
ICD 732.1, 733.4, 736.8, 765.1
Expanded minimum 1333 cases; rate 3438.2 p.m.l.b.

22. Congenital Dislocatable Hip (ICD 754.9) (See Table A1.7)
Period of choice: 1974-83
Cases with single diagnosis: 622
Minimum estimate of rate: 1604.3 per million live births
Cases accepted with 2 or more diagnoses: 12
Second (or more) diagnoses present in the 12 additional cases:
ICD 280, 735.8, 675.1, 770.8, 772.8
Expanded minimum 634 cases; rate 1635.3 p.m.l.b

5.2. ADDITIONAL MULTIFACTORIALS

There are two ways in which the preceding count of multifactorial cases will be falsely low because of a simple inherent bias in the counting process that could be present whenever a case had more than one diagnosis.

(i) Since only those cases with a single diagnosis (or with essentially the same second or more diagnoses) were counted, the chance occurrence of a second non-multifactorial diagnosis occurring in the same individual has been ignored and these cases have not been included in the count.

(ii) Similarly the chance occurrence of a second, unrelated multifactorial diagnosis occurring in the same individual has been ignored.

Each of these possibilities has been examined:-

5.2.1 The Chance Occurrence of an Additional Non-Multifactorial Diagnosis.

Using the middle birth period (1964-1973) as the basis of the calculations:

Total number of single diagnosis cases (all causes)	19,746
Single-diagnosis multifactorial cases	10,963
(By Subtraction) Single diagnosis non-multifactorial cases	8,783

The probability of any one individual having a non-multifactorial diagnosis is therefore 8783 in 344,665 live births, or .02548.

In 10,963 multifactorials the number of cases that could be expected by chance to have a second, unrelated, non-multifactorial diagnosis is 10,963 x .02548 = 279, or 809.5 per million live births.

The previous estimate of the multifactorial rate should therefore be increased by approximately 809.5 per million live births.

5.2.2 The Chance Occurrence of an Additional Multifactorial Diagnosis

Again using the middle birth period (1964-1973) as the basis of the calculations:

Number of single-diagnosis multifactorial cases 10,963.

The probability of any one individual having a multifactorial diagnosis is therefore 10,963 in 344,665 live births, or .03181.

The number of cases with a single multifactorial diagnosis that could be expected, by chance, to have a second multifactorial diagnosis is:

10,963 x .03181 = 349, or 1,012.6 per million live births.

Combining these two figures and adding to the figure given earlier leads to an increase of 1,822.1 in the multifactorial rate, from 44,039.2 to 45,861.3 p.m.l.b.

5.2.3 Testing the Estimates

In the previous section, the probabilities of having by chance either an additional non-multifactorial or multifactorial diagnosis were examined from a theoretical perspective.

For interest, the actual observed occurrence of the second possibility (multiple multifactorials) has been determined.

First, a 22 x 22 matrix was prepared, a portion of which is shown in Table 5.3, and which is summarized in Table 5.4. As can be seen at the foot of Table 5.4, total counts need to be divided by 2 to allow for the fact that each case is represented twice. For comparison with the previous sections, it is appropriate to use the figures for the middle cohort (1964-73), which had a total count of 327 cases, and which, after dividing by 2, gives a rate of 1064.8 per million live births -- fairly close to the

Using the 'best' (usually the highest) rate by birth-year period for each diagnosis, the additional rate is 1696.4 p.m.l.b., an increase of some 40% over the 'simple' rate for the middle decade.

5.2.4. Triple Multifactorials

While the preceding paragraphs have been concerned with double multifactorials, there is also, of course, the possibility of triple, quadruple, etc. One would expect that the numbers would become vanishingly small as this sequence is followed, and in fact, Table 5.5 illustrates the substantially smaller numbers of triple compared to double multifactorial diagnoses that were found in the present data set. After adjustment, another 89.8 cases per million live-births can be added to the total multifactorial estimate, -- approximately 5% of the figure contributed by the double diagnosis cases. (In this case the adjustment consisted of dividing the strabismus rate by 2, and all others by six).

The contribution of quadruple (or more) diagnoses has not been considered.

Thus in terms of the original "expanded minimum" estimate of 43,986.9 multifactorial conditions per million live births (Table 5.2), the double multifactorial diagnoses contribute another 1696.4 (3.9%), and the triple another 89.8 (0.2%), which, when added to the non-multifactorial figure of 809.5 gives a final estimate of 46582.6 p.m.l.b. or 4.7%. This final estimate of 46582.6 p.m.l.b. is some 5.9% higher than the initial "expanded minimum figure" of 43986.9.

In the earlier study by Trimble and Doughty, the combined rate for Congenital Malformations and Other Multifactorial was 4.7%, adjusted upward to a final figure of 5.2%.

5.2.5 Genetic: Unknown Etiology

Although not strictly a part of the Multifactorial section, it is convenient to consider this group here, since most of the diagnoses so coded (Registry Etiology "01") were in fact strabismus. Thus of 3860 single diagnoses in the 1964-73 birth cohort, 3566 (92.4%) were strabismus. The non-strabismus diagnoses are summarized for all years in Appendix 3, Table A 3.7. Excluding strabismus, rates for the three birth-year periods were 1606.9, 1207.0, and 626.8.

Table 5.1

Multifactorial cases with only one diagnosis on their record
*Indicates special Registry code (see Appendix 1, Table A 1.7)

MULTIFACTORIAL CONDITIONS		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9		N	Rate	N	Rate	N	Rate	N	Rate
250	Diabetes Mellitus	526	1202.3	382	1108.3	103	265.7	1011	864.2
295	Schizophrenic Psychoses	181	413.7	1	2.9	0	0.0	182	155.6
296	Affective Psychoses	10	22.9	0	0.0	0	0.0	10	8.5
317.1*	Borderline Mental Retardation	314	717.7	63	182.8	1	2.6	378	323.1
317.2*	Mild Mental Retardation	181	413.7	37	107.4	5	12.9	223	190.6
345	Epilepsy	807	1844.6	502	1456.5	228	588.1	1537	1313.8
378 *	Strabismus	924	2112.0	3566	10346.3	1450	3740.0	5940	5077.5
493	Asthma	124	283.4	53	153.8	71	183.1	248	212.0
550	Inguinal Hernia	0	0.0	196	568.7	1997	5150.8	2193	1874.6
691.8	Eczema	37	84.6	4	11.6	3	7.7	44	37.6
740	Anencephaly	58	132.6	45	130.6	50	129.0	153	130.8
741	Spina Bifida	214	489.1	117	339.5	67	172.8	398	340.2
742	Encephalocele	5	11.4	7	20.3	8	20.6	20	17.1
742.3	Congenital Hydrocephalus	48	109.7	99	287.2	76	196.0	223	190.6
745-7	Congen Anom of Heart & Circ System	1177	2690.3	1699	4929.4	1734	4472.5	4610	3940.6
749	Cleft Palate & Cleft Lip	468	1069.7	445	1291.1	431	1111.7	1344	1148.8
750.5	Congenital Hypertropic Pyloric Stenosis	23	52.6	805	2335.6	909	2344.6	1737	1484.8
751.3	Hirschsprung's Diseases etc.	9	20.6	60	174.1	43	110.9	112	95.7
752.6	Hypospadias and Epispadias	102	233.1	558	1619.0	620	1599.2	1280	1094.1
754.7*	Clubfoot	679	1552.0	1433	4157.7	1967	5073.4	4079	3486.7
754.3	Congenital Dislocation of Hip	197	450.3	878	2547.4	1322	3409.8	2397	2048.9
754.9*	Congenital Dislocatable Hip	0	0.0	12	34.8	622	1604.3	634	541.9
TOTAL		6084	13906.2	10962	31804.8	11707	30195.6	28753	24577.9

Table 5.2

Multifactorial cases by period of choice. Rates are per million live births.
* Indicates special Registry code (see Appendix 1, Table A1.7)

MULTIFACTORIAL CONDITIONS		PERIOD OF CHOICE	MINIMUM (Single diag.)		ADDITIONAL (2 or more diag.)		EXPANDED MINIMUM	
ICD9			N	Rate	N	Rate	N	Rate
250	Diabetes Mellitus	1952-63	526	1202.3	37	84.6	563	1286.8
295	Schizophrenic Psychoses	1952-63	181	413.7	13	29.7	194	443.4
296	Affective Psychoses	1952-63	10	22.9	3	6.9	13	29.7
317.1*	Borderline Mental Retardation	1952-63	314	717.7	98	224.0	412	941.7
317.2*	Mild Mental Retardation	1952-63	181	413.7	78	178.3	259	592.0
345	Epilepsy (excluding 345.6)	1952-63	807	1844.6	39	89.1	846	1933.7
378 *	Strabismus	1964-73	3566	10346.3	27	78.3	3593	10424.6
493	Asthma	1952-63	124	283.4	27	61.7	151	345.1
550	Inguinal Hernia	1974-83	1997	5150.8	394	1016.2	2391	6167.1
691.8	Eczema	1952-63	37	84.6	0	0.0	37	84.6
740	Anencephaly	1974-83	50	129.0	9	23.2	59	152.2
741	Spina Bifida	1974-83	67	172.8	11	28.4	78	201.2
742.0	Encephalocele	1974-83	8	20.6	2	5.2	10	25.8
742.3	Congenital Hydrocephalus	1964-73	99	287.2	25	72.5	124	359.8
745-7	Congenital Anomalies of Heart & Circulatory System	1964-73	1699	4929.4	30	87.0	1729	5016.5
749	Cleft Palate & Cleft Lip	1964-73	445	1291.1	45	130.6	490	1421.7
750.5	Congenital Hypertropic Pyloric Stenosis	1974-83	909	2344.6	8	20.6	917	2365.2
751.3	Hirschsprung's Diseases etc.	1964-73	60	174.1	4	11.6	64	185.7
752.6	Hypospadias and Epispadias	1964-73	558	1619.0	70	203.1	628	1822.1
754.7*	Clubfoot	1974-83	1967	5073.4	16	41.3	1983	5114.7
754.3	Congenital Dislocation of Hip	1974-83	1322	3409.8	11	28.4	1333	3438.2
754.9*	Congenital Dislocatable Hip	1974-83	622	1604.3	12	31.0	634	1635.3
TOTAL			15549	41535.3	959	2451.7	16508	43986.9

Table 5.3

Part of 22 x 22 matrix of multifactorials

First Diagnosis	250			295			296			. . . etc.
Birth decade	1952-63	1964-73	1974-83	1952-63	1964-73	1974-83	1952-63	1964-73	1974-83	. . . etc.
Second Diagnosis										
250	--	--	--	0	1	0	0	0	0	
295	0	1	0	--	--	--	3	0	0	
296	0	0	0	3	0	0	--	--	--	
317.1	0	0	0	9	0	0	1	0	0	
317.2	1	0	0	7	1	0	0	0	0	
345	2	3	1	3	0	0	0	0	0	
378	2	1	0	3	0	0	0	0	0	
493	2	2	1	0	0	0	1	0	0	
550	0	0	1	0	0	1	0	0	0	
619.8	0	0	0	0	0	0	0	0	0	
.										
.										
.										
etc.										

Table 5.4

Frequency of double multifactorial conditions in same individuals

*Indicates special Registry code (see Appendix 1, Table A1.7)

DOUBLE MULTIFACTORIALS		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9		N	Rate	N	Rate	N	Rate	N	Rate
250	Diabetes Mellitus	12	27.4	10	29.0	5	12.9	27	23.1
295	Schizophrenic Psychoses	28	64.0	2	5.8	0	0.0	30	25.6
296	Affective Psychoses	5	11.4	0	0.0	0	0.0	5	4.3
317.1*	Borderline Mental Retardation	101	230.9	12	34.8	0	0.0	113	96.6
317.2*	Mild Mental Retardation	65	148.6	14	40.6	3	7.7	82	70.1
345	Epilepsy	125	285.7	60	174.1	38	98.0	223	190.6
378 *	Strabismus	89	203.4	103	298.8	67	172.8	259	221.4
493	Asthma	24	54.9	10	29.0	11	28.4	45	38.5
550	Inguinal Hernia	2	4.6	41	119.0	111	286.3	154	131.6
691.8	Eczema	0	0.0	0	0.0	0	0.0	0	0.0
740	Anencephaly	10	22.9	9	26.1	6	15.5	25	21.4
741	Spina Bifida	61	139.4	30	87.0	20	51.6	111	94.9
742	Encephalocele	1	2.3	4	11.6	6	15.5	11	9.4
742.3	Congenital Hydrocephalus	10	22.9	22	63.8	24	61.9	56	47.9
745-7	Congen Anom of Heart & Circ System	79	180.6	111	322.1	139	358.5	329	281.2
749	Cleft Palate & Cleft Lip	38	86.9	49	142.2	42	108.3	129	110.3
750.5	Congenital Hypertropic Pyloric Stenosis	4	9.1	40	116.1	35	90.3	79	67.5
751.3	Hirschsprung's Diseases etc.	1	2.3	3	8.7	5	12.9	9	7.7
752.6	Hypospadias and Epispadias	13	29.7	39	113.2	47	121.2	99	84.6
754.3	Congenital Dislocation of Hip	13	29.7	57	165.4	89	229.6	159	135.9
754.7*	Clubfoot	97	221.7	117	339.5	143	368.8	357	305.2
754.9*	Congenital Dislocatable Hip	0	0.0	1	2.9	35	90.3	36	30.8
TOTAL		778	1778.3	734	2129.6	826	2130.5	2338	1998.5
SUM OF HIGHEST INDIVIDUAL RATES DIVIDED BY 2 TO AVOID DOUBLE COUNTING									1547.0

Table 5.5

Frequency of triple multifactorial conditions in same individuals

*Indicates special Registry code (see Appendix 1, Table A1.7)

TRIPLE - MULTIFACTORIALS		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9		N	Rate	N	Rate	N	Rate	N	Rate
250	Diabetes Mellitus	0	0.0	1	2.9	1	2.6	2	1.7
295	Schizophrenic Psychoses	3	6.9	0	0.0	0	0.0	3	2.6
296	Affective Psychoses	0	0.0	0	0.0	0	0.0	0	0.0
317.1*	Borderline Mental Retardation	7	16.0	1	2.9	0	0.0	8	6.8
317.2*	Mild Mental Retardation	5	11.4	4	11.6	0	0.0	9	7.7
345	Epilepsy	4	9.1	6	17.4	4	10.3	14	12.0
378 *	Strabismus	9	20.6	11	31.9	5	12.9	25	21.4
493	Asthma	1	2.3	1	2.9	0	0.0	2	1.7
550	Inguinal Hernia	0	0.0	2	5.8	0	0.0	2	1.7
691.8	Eczema	0	0.0	0	0.0	0	0.0	0	0.0
740	Anencephaly	0	0.0	0	0.0	2	5.2	2	1.7
741	Spina Bifida	7	16.0	7	20.3	11	28.4	25	21.4
742	Encephalocele	1	2.3	1	2.9	4	10.3	6	5.1
742.3	Congenital Hydrocephalus	1	2.3	3	8.7	3	7.7	7	6.0
745-7	Congen Anom of Heart & Circ System	7	16.0	6	17.4	3	7.7	16	13.7
749	Cleft Palate & Cleft Lip	4	9.1	4	11.6	3	7.7	11	9.4
750.5	Congenital Hypertropic Pyloric Stenosis	1	2.3	2	5.8	1	2.6	4	3.4
751.3	Hirschsprung's Diseases etc.	0	0.0	0	0.0	0	0.0	0	0.0
752.6	Hypospadias and Epispadias	3	6.9	3	8.7	0	0.0	6	5.1
754.7*	Clubfoot	11	25.1	9	26.1	12	31.0	32	27.4
754.3	Congenital Dislocation of Hip	3	6.9	6	17.4	9	23.2	18	15.4
754.9*	Congenital Dislocatable Hip	0	0.0	1	2.9	1	2.6	2	1.7
TOTAL		67	153.1	68	197.3	59	152.2	194	165.8
SUM OF HIGHEST INDIVIDUAL RATES DIVIDED BY 3 TO AVOID MULTIPLE COUNTING									82.8

CHAPTER 6 CONGENITAL ANOMALIES

As explained earlier, in this analysis Congenital Anomalies were not considered as part of the hierarchical system, since they are, by definition, related less to etiology than to time of appearance.

Table 6.1 summarizes the information presented in the earlier "etiology" chapters for conditions having ICD numbers in the Congenital Anomaly range, 740.0 to 759.9. Detailed figures may be found in Appendix Tables A 3.1 to A 3.6. Once again, as in Table 4.1, ICD 758.4 should be discounted in Table A 3.4.

In the case of the Multifactorials, the "expanded minimum" figure shown in Table 5.2 was subsequenty increased by 5.9% (from 43986.9 to 46582.6 p.m.l.b.) due to the addition of the "double" etc adjustments described on pages 29 and 30. The figure of 21790.4 in Appendix Table A 3.6 should therefore be increased by 5.9%, giving an adjusted rate of 23076.0 p.m.l.b. in Table 6.1.

In addition, Genetic Unknown cases accounted for an extra 564.6 p.m.l.b.

The overall rate for cases with a genetic etiology of some kind was thus 26609.4 per million live births, with 11% contributed by the single-gene and chromosome disorders, 87% by the multifactorial conditions and 2% by genetic conditions of unknown etiology. However, for all cases <u>including</u> those to which no genetic etiology has been attributed in this study, the combined rate in the decade with the best ascertainment was about twice as great, i.e. 52,808.2 per million live births (Table 6.2).

To compare these figures with those obtained by Trimble and Doughty in their earlier study of this data source[36], it is necessary to recognize that after single-gene and chromosome disorders had been counted (and thus removed from consideration) their next category was "Congenital Malformations" which yielded a "minimal" rate of 3.580%. After removal of these cases, "Other Multifactorial" were counted, and a minimal rate of 1.582% was found. These rates were subsequently adjusted to 4.28 and 4.73% to allow for incomplete ascertainment. However, Trimble and Doughty viewed all congenital anomalies as probably having some sort of genetic or partially genetic etiology. They therefore did not attempt to separate out a non-genetic category of congenital anomalies as we have done here.

In the present analysis we have <u>first</u> counted 22 selected Multifactorials (43986.9 p.m.l.b. before adjusting for multiple diagnoses, Table 5.2), and of these, Congenital Anomalies accounted for 50% (21,790.4 p.m.l.b., Table 6.1).

Our lower figure for total Multifactorials, and subset of Congenital Anomalies, is due largely to our exclusion of about half of all congenital anomalies as being possibly non-genetic. Trimble and Doughty did not do this, but instead treated all Congenital Anomalies as probably having some sort of genetic or partial genetic cause. Our exclusions are in part the result of restricting the counts of multifactorials to only 22 major conditions, thus excluding such things as polydactyly and syndactyly. As well, some Congenital Anomalies were not counted by us because they had an identifiable environmental cause, and others because the cause was unknown. Appearance later in life (part of the justification for the upward adjustment in the Trimble analysis) should presumably be less of a problem in the present analysis, since a longer follow-up exists, – although maximum rates for some of these conditions are in the youngest cohort, born in 1974-83 probably indicating better ascertainment, and/or earlier diagnosis (e.g. Dislocation of Hip, for which there are now active screening programmes in some parts of the province).

For completeness, we have also counted the total number of occasions that a diagnosis of congenital malformation (ICD 740.0 - 759.9) appeared in the Registry files. These numbers and rates are shown in Tables 6.2 to 6.5.

It should be noted that no attempt has been made in these tables to deal with the problem of individuals with two or more such diagnoses on their record. The numbers in the body of the tables are for <u>diagnoses</u> and therefore over-estimate the number of individuals involved. The figure for <u>cases</u> is given at the bottom of each table. (Note also that these tables include the individuals previously counted in the "etiological" chapters).

The average number of diagnoses per case has risen over the years, but not substantially, given the great increase in the number of diagnoses that can now be listed. Thus in the 1952-63 period there were 1.23 diagnoses per case, 1.27 in the middle period, and 1.30 in the last. Inverting these figures for the three decades, the number of cases as a percentage of total diagnoses were 81%, 79%, and 77%. As a very crude first step, diagnoses might therefore be adjusted downward to about 80%, to give a rate reflecting a case rate.

Table 6.1

Summary table of Congenital Anomalies, by etiology

CONGENITAL ANOMALIES	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE								SUM OF HIGHEST IND. RATES
	1952-63		1964-73		1974-83		TOTAL		
	N	Rate	N	Rate	N	Rate	N	Rate	
Dominant Conditions	202	461.7	198	574.5	181	466.8	581	496.6	741.5
Recessive Conditions	52	118.9	71	206.0	74	190.9	197	168.4	290.3
X-Linked Conditions	10	22.9	13	37.7	20	51.6	43	36.8	66.4
Autosomal Chromosome Conditions	597	1364.6	529	1534.8	538	1387.7	1664	1442.4	1718.3
Sex Chromosomal Conditions	64	146.3	39	113.2	33	85.1	136	116.3	152.3
SUB-TOTAL									2968.8
Multifactorial Conditions	-	-	-	-	-	-	-	-	23076.0
Genetic: Unknown Etiology	247	564.6	176	510.6	116	299.2	539	460.7	564.6**
TOTAL									26609.4

** The rate of 564.6 p.m.l.b. for Genetic unknown is based on the highest decade rate, not on the sum of highest individual diagnosis rates.

Table 6.2

Congenital Anomalies: total diagnoses by ICD category and birth period, plus total cases by birth period only
Rates are per million live births.
*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD9		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
740	Anencephaly	74	169.1	60	174.1	89	229.6	223	190.6
741	Spina Bifida	377	861.7	267	774.7	261	673.2	905	773.6
742.0	Encephalocoele	12	27.4	26	75.4	46	118.6	84	71.8
742.3	Congenital Hydrocephalus	182	416.0	273	792.1	347	895.0	802	685.5
740-2	Other Nervous System	158	361.1	268	777.6	372	959.5	798	682.1
743	Eye	382	873.1	507	1471.0	603	1555.3	1492	1275.4
744	Ear, Face, Neck	158	361.1	626	1816.3	858	2213.0	1642	1403.6
745-7	Heart and Circulation	1981	4528.0	3628	10526.2	5073	13084.7	10682	9130.9
748	Respiratory	38	86.9	748	2170.2	748	1929.3	1534	1311.3
749	Cleft palate and lip	812	1856.0	757	2196.3	809	2086.6	2378	2032.7
750.5	Pyloric stenosis	38	86.9	900	2611.2	1063	2741.8	2001	1710.4
751.3	Hirschprung dis, etc	16	36.6	81	235	89	229.6	186	159.0
750-1	Other Digestive System	212	484.6	667	1935.2	1277	3293.7	2156	1842.9
752.6	Hypospadias	174	397.7	788	2286.3	990	2553.5	1952	1668.6
752-3	Other Genito-Urinary	421	962.3	2866	8315.3	3369	8689.6	6656	5689.5
754.7*	Clubfoot	1065	2434.3	1896	5501.0	2694	6948.6	5655	4833.9
754.3*	Congen Dislocation Hip	313	715.4	1109	3217.6	1713	4418.3	3135	2679.8
754.9	Congen Dislocatable Hip	4	9.1	23	66.7	779	2009.3	806	689.0
754-6	Other Musc. Skeletal	1255	2868.6	2256	6545.5	3261	8411.0	6772	5788.7
757	Integument	227	518.9	678	1967.1	1165	3004.9	2070	1769.4
758	Chromosomal Anomalies	665	1520.0	574	1665.4	630	1624.9	1869	1597.6
759	Other	137	313.1	248	719.5	424	1093.6	809	691.5
	Total Diagnoses	8701	19887.8	18671	54171.4	26660	68763.6	54032	46186.2
	Total Cases	7065	16148.4	14707	42670.4	20474	52808.2	42246	36111.6

Table 6.3

Congenital Anomalies (1952-63): total diagnoses by etiology coding on Registry data base

*Indicates special Registry code (see Appendix 1, A1.7)

ICD9		Genetic							Cong Anom	Perinatal etc.	Etiol Unknown	Total
		Dom	Rec	X-link	Auto Chrom	Sex Chrom	Multi-Fact	Unspec Genetic				
740	Anencephaly	0	0	0	0	0	69	4	1	0	0	74
741	Spina Bifida	0	0	0	0	0	358	4	12	0	3	377
742.0	Encephalocoele	0	0	0	0	0	1	0	8	0	3	12
742.3	Congenital Hydroceph	1		1	0	0	0	5	168	4	4	182
(740-2)	Other Nervous System	0	6	1	2	0	1	0	114	11	22	157
743	Eye	34	12	2	1	1	0	19	254	27	32	382
744	Ear, Face, Neck	2	0	2	1	1	1	2	121	9	19	158
745-7	Heart and Circulation	16	1	0	11	1	1592	46	79	30	205	1981
748	Respiratory	1	0	0	0	0	2	2	30	0	3	38
749	Cleft Palate and Lip	0	3	0	1	0	687	45	57	2	17	812
750.5	Pyloric Stenosis	0	0	0	0	0	38	0	0	0	0	38
751.3	Hirschprung dis, etc	0	0	0	0	0	14	0	2	0	0	16
(750-1)	Other Digestive Syste	2	0	0	2	0	0	2	183	0	23	212
752.6	Hypospadias	1	1	0	0	0	0	5	152	0	15	174
(752-3)	Other Genito-Urinary	5	14	3	0	2	1	12	320	1	63	421
754.7*	Clubfoot	1	2	0	0	0	893	43	79	2	45	1065
754.3*	Congen Dislocation Hip	0	1	0	0	0	264	18	16	1	13	313
754.9	Congen Dislocatable Hi	0	0	0	0	0	4	0	0	0	0	4
(754-6)	Other Musc. Skeletal	127	12	5	2	1	13	35	859	17	184	1255
757	Integument	11	11	3	0	0	2	5	178	0	17	227
758	Chromosomal anomalie	0	0	0	592	67	1	0	3	0	2	665
759	Other	45	9	2	0	1	0	1	61	0	18	137
	TOTAL DIAGNOSES	246	72	19	612	74	3941	248	2697	104	688	8701
	TOTAL CASES											7065

Table 6.4

Congenital Anomalies (1964-73): total diagnoses by etiology coding on Registry data base

*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD9		Genetic							Cong Anom	Perinatal etc.	Etiol Unknown	Total
		Dom	Rec	X-link	Auto Chrom	Sex Chrom	Multi-Fact	Unspec Genetic				
740	Anencephaly	0	0	0	0	0	57	0	3	0	0	60
741	Spina Bifida	0	0	0	0	0	250	0	12	2	3	267
742.0	Encephalocoele	0	1	0	0	0	0	1	21	1	2	26
742.3	Congenital Hydroceph	2	5	1	0	0	3	1	240	1	20	273
(740-2)	Other Nervous System	1	8	2	4	0	1	8	193	15	36	268
743	Eye	19	21	5	2	0	0	6	365	39	50	507
744	Ear, Face, Neck	2	0	2	3	1	0	5	553	3	57	626
745-7	Heart and Circulation	13	9	1	46	1	2661	21	213	86	577	3628
748	Respiratory	0	1	0	1	0	2	2	138	1	28	173
749	Cleft Palate and Lip	5	3	0	10	0	613	21	73	6	26	757
750.5	Pyloric Stenosis	0	1	0	0	0	886	0	12	0	1	900
751.3	Hirschprung dis, etc	0	1	0	0	0	64	0	14	0	2	81
(750-1)	Other Digestive Syste	2	5	0	8	0	5	0	585	5	57	667
752.6	Hypospadias	2	1	1	1	1	0	8	755	2	17	788
(752-3)	Other Genito-Urinary	7	26	3	4	0	0	20	2581	11	214	2866
754.7*	Clubfoot	4	1	0	6	0	1717	12	118	5	33	1896
754.3*	Congen Dislocation Hip	3	3	0	2	0	1032	7	41	5	16	1109
754.9	Congen Dislocatable Hi	0	0	0	0	0	20	0	1	1	1	23
(754-6)	Other Musc. Skeletal	139	24	3	12	0	33	44	1765	14	222	2256
757	Integument	6	5	4	0	0	2	7	618	3	33	678
758	Chromosomal anomalie	0	0	0	528	40	1	0	1	0	4	574
759	Other	52	14	0	0	0	3	10	138	1	30	248
	TOTAL DIAGNOSES	257	129	22	627	43	7350	173	8440	201	1429	18671
	TOTAL CASES											14707

Table 6.5

Congenital Anomalies (1974-83): total diagnoses by etiology coding on Registry data base

*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD9		Genetic							Cong Anom	Perinatal etc.	Etiol Unknown	Total
		Dom	Rec	X-link	Auto Chrom	Sex Chrom	Multi-Fact	Unspec Genetic				
740	Anencephaly	0	0	0	0	0	85	0	4	0	0	89
741	Spina Bifida	0	1	0	1	0	218	0	36	2	3	261
742.0	Encephalocoele	0	1	0	0	0	6	0	36	0	3	46
742.3	Congenital Hydroceph	3	3	0	3	0	7	3	290	17	21	347
(740-2)	Other Nervous System	7	5	2	14	0	5	5	269	27	38	372
743	Eye	22	11	5	17	0	0	7	470	26	45	603
744	Ear, Face, Neck	6	6	1	10	1	3	2	774	10	45	858
745-7	Heart and Circulation	9	31	0	187	7	2995	7	805	93	939	5073
748	Respiratory	5	8	0	6	0	6	1	555	4	163	748
749	Cleft Palate and Lip	3	7	1	27	1	649	4	95	6	16	809
750.5	Pyloric Stenosis	0	1	0	1	0	1017	1	38	0	5	1063
751.3	Hirschprung dis. etc	0	1	0	1	0	79	0	7	0	1	89
(750-1)	Other Digestive Syste	3	6	1	19	1	11	4	1140	1	91	1277
752.6	Hypospadias	2	3	1	4	1	0	4	963	5	7	990
(752-3)	Other Genito-Urinary	6	27	4	20	6	7	27	3049	11	212	3369
754.7*	Clubfoot	4	8	1	10	0	2459	6	147	8	51	2694
754.3*	Congen Dislocation Hip	4	3	2	6	0	1613	3	59	2	21	1713
754.9	Congen Dislocatable Hi	1	0	0	3	0	744	0	28	0	3	779
(754-6)	Other Musc. Skeletal	136	44	6	55	2	67	65	2605	43	238	3261
757	Integument	12	12	10	7	0	2	12	1065	5	40	1165
758	Chromosomal anomalie	0	0	0	577	37	3	0	4	2	7	630
759	Other	41	18	3	1	0	5	4	278	7	67	424
	TOTAL DIAGNOSES	264	196	37	969	56	9981	155	12717	269	2016	26660
	TOTAL CASES											20474

CHAPTER 7 EFFECT OF PREGNANCY TERMINATION

In utero diagnosis of genetic abnormality has become increasingly common in recent years, and this could bias the estimates of genetic defect in liveborn children, since a positive test may lead to termination of the pregnancy.

The potential impact has been calculated from the records of the UBC pre-natal screening clinic, and is illustrated in Tables 7.1 and 7.2.

The figures for possible impact on maximum apparent incidence rates resulting from pregnancy termination will be an over-estimate because:

i) The maximum losses are for the birth period 1974-83 (and are virtually zero for the other birth periods), whereas the estimates of incidence arrived at earlier in this report are based mainly on the first and second birth periods.

ii) Not all the affected fetuses would have survived to be born alive

Thus the impact of pregnancy terminations has been extremely small.

Table 7.1

Potential impact of pregnancy termination on the apparent incidence of genetic disease and non-genetic congenital malformations reported in previous chapters

	Highest Rates (percent)	
	Previous Estimates (this study)	Maximum incidence of terminations
Dominant	.14	.0003
Recessive	.17	.0013
X-linked	.05	.0039
Chromosomal	.19	.0178
Multifactorial		
a) Congenital	2.2	.0039
b) Other	2.2	0
Total	4.95	.0272

Table 7.2

Genetic Defects Found Following Pregnancy Terminations

Categories	ICD 9	Conditions	Counts and Rates (per million) by birth year range							
			1952-1963		1964-1973		1974-1983		Total	
			N	Rate	N	Rate	N	Rate	N	Rate
Dominant	359.2	Myotonic dystrophy	0	0.0	0	0.0	1	2.6	1	2.6
		Subtotal	0	0.0	0	0.0	1	2.6	1	2.6
Recessive	271.0	Pompe disease	0	0.0	0	0.0	1	2.6	1	2.6
	330.0	Krabbe disease	0	0.0	0	0.0	1	2.6	1	2.6
	--	Biochemical errors	0	0.0	0	0.0	3	7.7	3	7.7
		Subtotal	0	0.0	0	0.0	5	12.9	5	12.9
Sex Linked	286.0	Hemophilia (male)	0	0.0	0	0.0	1	2.6	1	2.6
	359.1	Duchene muscular dystrophy	0	0.0	0	0.0	9	23.2	9	23.2
	742.3	Hydrocephalus, sex linked	0	0.0	0	0.0	3	7.7	3	7.7
	759.8	Menkes syndrome	0	0.0	0	0.0	1	2.6	1	2.6
	--	X-linked disorder	0	0.0	0	0.0	1	2.6	1	2.6
		Subtotal	0	0.0	0	0.0	15	38.7	15	38.7
Chromosomal	758.0	Down syndrome	0	0.0	2	5.8	32	82.5	34	88.3
	758.1	Trisomy 13	0	0.0	0	0.0	7	18.1	7	18.1
	758.2	Trisomy 18	0	0.0	0	0.0	10	25.8	10	25.8
	758.5	46 plus ring chromosome	0	0.0	0	0.0	2	5.2	2	5.2
	758.5	Deletion of chromosome 15	0	0.0	0	0.0	1	2.6	1	2.6
	758.5	Mosaic trisomy	0	0.0	0	0.0	1	2.6	1	2.6
	758.5	Unbalanced translocation	0	0.0	0	0.0	2	5.2	2	5.2
	758.6	Turner syndrome	0	0.0	0	0.0	6	15.5	6	15.5
	758.7	Kleinfelter syndrome	0	0.0	0	0.0	5	12.9	5	12.9
	758.8	Triple X females	0	0.0	0	0.0	3	7.7	3	7.7
		Subtotal	0	0.0	2	5.8	69	178.0	71	183.8
Multifactorial Cong. Anomaly	740-42	Neural tube defects	0	0.0	0	0.0	14	36.1	14	36.1
	--	Amniotic band syndrome (McK 21710)	0	0.0	0	0.0	1	2.6	1	2.6
		Subtotal	0	0.0	0	0.0	15	38.7	15	38.7
		TOTAL	0	0.0	2	5.8	105	270.8	107	276.6

CHAPTER 8 DISCUSSION AND RECOMMENDATIONS

The results of the present analysis of data from the British Columbia Health Surveillance Registry for 1952-83 are in general rather similar to those obtained in an earlier analysis of data to 1972 from the same Registry. This similarity is reassuring in view of the many improvements in the Registry since 1973 as described in Chapter 2. There are however some differences and limitations in the results of the two analyses which are discussed in more detail.

1. Congenital anomalies

Previous studies have treated the congenital anomalies defined by ICD codes 740-759 as being all "potentially genetic or partially genetic". Such earlier treatments tended to ignore known admixtures of environmentally caused anomalies plus cases of unknown etiology. To correct for this bias, considerable effort was devoted in the present study to counting just those cases for which there was believed to be a significant polygenic component in the causation. All others have been excluded from the data for ICD codes 740-759, and the frequencies in a birth cohort have been reduced accordingly. This reduction should not be confused with failure to ascertain cases.

Table 8.1 compares data on incidence of all congenital anomalies of potential genetic or partially-genetic origin from the present analysis with those from the previous analysis of B.C. data and those from a recent analysis of Hungarian data[11]. (For ease of comparison, in this section the data are expressed per thousand rather than per million live-births as used in previous sections). Data from a U.S. study are also available[25,42,43] but are expressed in somewhat different terms. The Hungarian and earlier B.C. data are expressed as frequencies of all live-births with one or more congenital anomalies listed by ICD category (Table 8.1) and in terms of the the present B.C. data are expressed both in terms of the 22 selected ICD categories, and in terms of the overall frequency of diagnoses appearing in the Registry. Note that a crude adjustment factor of 0.8 has been applied in an attempt to make the rates more comparable to case rates, since the number of cases in each birth-period was approximately 80% of the total number of diagnoses - see previous chapter.

Some of the differences between the earlier and the present analysis of the B.C. data (Table 8.1) are due to our decision to exclude congenital anomalies in certain ICD categories, notably 743, 744, 748, 753, and 755 to 759, from the list of 22 major diseases with potential multifactorial etiology (Chapter 5). Although this would not have a major impact on total numbers of multifactorial diseases, it does alter the results on incidence of genetic or partially-genetic origin.

It is of interest that the incidence of congenital anomalies in ICD category 754.3 and 754.9 has increased appreciably over the past 3 decades (Table 5.1), presumably due to increased diagnostic ascertainment by examining physicians. The most recent value in B.C. appears to be somewhat lower than the incidence reported in the prospective U.S. study in1974[42,43] and is still much lower than the value observed in Hungary (Table 8.1), where congenital dislocation of the hip accounts for 43% of all congenital anomalies. The high incidence of congenital dislocation of the hip reported from Hungary may be due in part to local genetic and environmental factors, or to inclusion of less severe hip problems. (The latter might be due to a number of factors: for example, testing at an earlier age, since it is known that testing tends to yield higher incidence rates the younger the children being tested).

The reported incidence of inguinal hernia (ICD 550), which is considered by many teratologists to belong in the category of congenital anomalies[43], has also increased markedly over the past 3 decades in B.C. (Table 5.1 and 8.1). This increase may also be due to improved diagnostic ascertainment and improved reporting to the B.C. Registry. On the basis of considerations such as the above, the use of the highest incidence rates reported for the three successive decades in B.C. would seem appropriate in this category as well as for other genetic or partially-genetic diseases.

Because the present data for ICD codes 740-759 exclude cases not thought to be polygenic, the combined rate for a birth cohort is expected to be lower than reported from previous studies. This is in fact what is observed in Tables 8.1 and 8.2.

2. Influence of age at onset on severity of symptoms

Most of the registrants in the earliest (1952-63) period of the present study would have reached an age of about 25 (maximum 31) years by the end of the Registry updates in 1983. This creates a serious underestimation of those genetic diseases whose onset and potential diagnosis is late in life. At the moment, this underestimation is believed to be most serious in the case of dominant genetic conditions (Table 3.1 and 8.2). Two examples might be cited. Huntington's chorea (ICD 333.4) was found in the present analysis to have an incidence rate of 16 per million live-births for persons in B.C. born between 1952 and 1963, with zero incidence reported for births in more recent decades (Table A2.2). The average age at onset of Huntington chorea is 41-45 years; only about 3% of all cases are diagnosed before age 25[44]. Thus the actual incidence of Huntington chorea over the whole population of all ages is closer to 400 than to 16 per million live-births[37,44]. Another example is monogenic familial hypercholesteremia (included in ICD 272). The incidence of all cases reported under ICD 272 in the present study was less than 40 per million live-births; the true incidence of dominant hypercholesteremia is believed to be closer to 2000 per million live-births when cases diagnosed after age 25 are included[37,44].

The total incidence of dominant diseases including those of late onset is believed to be about 7 per 1000 live births[37,44]. For this reason, international scientific committees did not rely upon estimates of incidence of dominant genetic diseases obtained from the earlier study of data for children in the B.C. Registry (Table 8.2).

The present study of incidence of dominant conditions in the B.C. Registry is providing higher numbers as the initial cohort grows older (Table 3.1); however, a detailed study of increase in incidence of many of the dominant disorders with age would be required to provide more reliable estimates of lifetime incidence of these dominant disorders.

Although a complete listing of all dominant disorders is required for assessment of the impact on health of the general population, the dominants of major importance for assessment of the effect of increased mutation rates are those of early onset which are included in Tables 3.1 and 8.2. The most common dominants of late onset are, as noted earlier, not maintained by high mutation rates; investigators were, for example unable to find a single clear case of a new mutation among several thousand Huntington chorea patients[44]. New mutations are believed to be responsible for most of the cases of dominant disorders (e.g. achondroplasia) with severe effects on the health of children[44]. The fraction of all dominant disorders (including those of late onset) which are due to new mutations in each generation is currently believed to be about 15%[42,43].

The United Nations scientific committee used the adjusted values for incidence of recessive disorders in the earlier B.C. study as the best estimate available in 1977 (Table 8.2). This estimate was later increased from 1.1 to 2.5 per 1000 live-births on the basis of other considerations. The suggested increase is supported by the unadjusted value of 1.7 per 1000 live-births obtained in the present study; and adjustment of the present B.C. data for incomplete ascertainment would be useful in order to obtain more accurate figures.

Similar problems of incomplete ascertainment apply to the present data on disorders attributed to changes in chromosome number (Table 8.2). On the basis of highest 10-year incidence rates, Down syndrome (ICD 758-0) would account for 71% and Klinefelter syndrome (ICD 758.7) for 3% of the total recorded for these diseases of chromosomal etiology in the present study (Tables 4.1 and 4.2). The recorded values for Klinefelter syndrome are undoubtedly much too low; the true incidence should be at least as high as that for Down syndrome[41,44]. The low incidence recorded for Klinefelter syndrome in both studies of B.C. data probably reflects the relatively minor nature of the health problems associated with Klinefelter as compared to Down syndrome; thus the fraction of all cases brought to the attention of diagnosing physicians will be much smaller in the case of Klinefelter than of

Down syndrome. As will be noted below, this underestimation of chromosomal diseases probably has little significance for assessment of genetic effects of exposure to low doses of radiation or other mutagenic agents, since these exposures are thought to produce little or no increase in the genetic diseases attributable to changes in chromosome number[42,43].

The last rows in Table 8.2 are concerned with genetic or partially-genetic diseases of multifactorial origin. The incidence of these diseases given in reports of international and national scientific committees since 1974 is the adjusted incidence obtained in the first analysis of the B.C. Registry data. The unadjusted totals obtained in the present study are similar to those obtained in the first report on the B.C. data.

It would in general seem fair to conclude that the results of the present analysis provide the basis for an improved estimate of the incidence of the genetic or partially-genetic diseases with serious health consequences in children and young adults before about age 25. The methodology used in the present study does however, lead to a lower estimate of those congenital anomalies of potential genetic or partially-genetic origin. The incidence of genetic diseases with minor health consequences, and the incidence of genetic diseases with late onset in life cannot be determined from these data. Within these limitations, the results of the present study provide a valuable update on the earlier study of the incidence of genetic disorders in chidlren and young adults.

3. Relevance to assessment of health hazards of mutagenic agents

The relative importance of the various classes of genetic disorders to assessment of the potential health hazards of low levels of ionizing radiation or other environmental mutagens is suggested by the data given in Table 8.3. Dominant mutations (Table 3.1), which are grouped together with X-linked recessive mutations (Table 3.3) for consideration of the impact of an increased mutation rate, are usually considered to provide the most important contribution to any increase in incidence of genetic diseases in the population resulting from exposure to environmental mutagens. Contributions from other recessive mutations (Table 3.2) are smaller and would not be evident for many generations. Current thinking suggests that genetic diseases attributable to alterations in chromosome number (Tables 4.1 and 4.2) would not be increased appreciably by exposure to low levels of radiation or other environmental mutagens. Small increases in incidence of genetic disorders would result from induced changes in chromosomal structure, notably unbalanced translocations. Diseases attributable to these structural chromosomal anomalies may be of diverse nature and do not at the present time appear to be restricted to particular ICD cateogries.

The contribution from partially-genetic disorders of multifactorial origin (Tables 5.1 and 5.2) represents a continuing problem which will presumably not be solved in the near future. In the first place, it is uncertain how the incidence of these multifactorial disorders would be affected, if at all, by an increase in normal rates of mutation. Recent UNSCEAR reports have assumed that about 5% of these multifactorial diseases will respond to increased mutation rates in a manner similar to that of monogenic dominant diseases; the 1980 BEIR report assumed, on the other hand, a mutational component of 5% to 50%. The differences in these assumptions can result in considerable variations in the relative importance of multifactorial diseases for assessment of the potential health hazards of environmental mutagens.

A second problem is the incidence of multifactorial disorders over the whole life-span of the population. Although the value of 90 per 1000 live-births for all multifactorial disorders (including congenital anomalies) in children has been widely accepted (Table 8.2), this value would be increased to about 600 per 1000 if multifactorial disorders of late onset (for example thyrotoxicosis, adult diabetes, psychoses, hypertension, myocardial infarction, ulcers) were included[43]. Inclusion of certain cancers would further increase the total incidence of multifactorial diseases. Despite these uncertainties, multifactorial diseases which become evident in children or young adults (Tables 5.1 and 5.2) would continue to have the largest personal health impact in terms of years of life lost or years of impaired life.

Some well organized population based Registries are quite effective at registering young people who are actually sick or handicapped. For the purpose of assessing genetic harm to health these individuals are particularly relevant. What is not generally recognized is that the omission of "cases" who are not noticeably affected, helps, rather than hinders, assessment of the actual harm from genetic disease. In the present data, the further exclusion of individuals with congenital anomalies where there is little evidence of a genetic or polygenic component in the causation represents an additional refinement.

In summary, approximately 54 per 1000 (5.4%) of individuals can be expected to demonstrate genetic or partially genetic diseases before about age 25. Single gene disorders are responsible for at least 3.6 per thousand, chromosomal disorders for 1.9 per thousand, and multifactorial for by far the greatest number, approximately 47 per thousand, with a further 1.2 per thousand due to genetic causes of unknown etiology.

Data are also presented on all congenital anomalies and 52.8 per thousand live births have been observed in the most recent birth period (Table 6.2, 1974-83). If this figure is included in the genetic load figure (as most other studies have done), the total is increased to 8.0%, rather than 5.4%. (The figure of 8.0% is arrived at by

adding half of 52.8 to 53.7, since 50% of congenital anomalies were counted by our definition of multifactorial).

4. Recommendations

A number of recommendations might be noted which stem from consideration of the above data and of the possible social implications of these data.

4.1. Although probable reasons for marked changes in reported incidence of certain disorders from one decade to another have been suggested in the discussion above, more direct evidence to support these suggestions (or not) would be highly desirable. This evidence would assist in assessment of the degree of underestimation of the incidence of various genetic disorders.

4.2. The B.C. Registry contains some 62,500 records of persons born before 1952 which were not included in the present study (see Chapter 2). These records could be used in an extension of the present study to determine the incidence of genetically affected individuals in older birth cohorts. In this proposed extension of the study, consideration must be given to the poorer ascertainment of certain disorders in earlier years (see item 2 above), dilution with cases born outside the province, losses due to migration and losses due to death. This extension of the present study if it were feasible, would again assist in assessment of underascertainment due to omission of many cases which are only diagnosed in older persons. The data in the Registry may not, however, be adequate to yield meaningful results in this age group.

4.3. The Registry records tabulated in the present study could be linked to death records in order to obtain age-specific death rates for the various categories of genetic disorders. The data would provide one objective criterion for estimation of the social burden caused by the existence of various genetic diseases. The registry records could also be linked to hospital admission records in order to obtain further information on number of days hospital stay per 100 affected children with certain kinds of heriditary disorder. The purpose of this type of linkage would again be an assessment of the social impact of these disorders. In this case, underascertainment of diseases with minor health effects is of less importance since these latter diseases add little to the total social burden. Preliminary studies along these lines were carried out earlier by Trimble and Smith[37]; considerably more information has been added to the various records since that time.

4.4. In order to assess the health effects of increased mutation rates resulting from exposure to radiation or other environmental mutagens, further data on the contribution of new mutations to the observed incidence of various multifactorial disorders is urgently required.

Table 8.1

Comparison of incidence of various congenital anomalies in three studies, with and without exclusion of non-polygenic cases

ICD9 code	Type of anomaly	Incidence per 1000 live births					
		Hungary (all cases)	B.C. 1967-69 (all cases)	B.C. 1952 - 83			
				Sum of highest rates: selected diag. categories	All Cases (d)		
					1952-63	1964-73	1974-83
740-742	Central nervous system	2.2	1.7	1.1	1.5	2.1	2.3
743	Eye	0.3	0.8	0.12 (a)	0.7	1.2	1.2
744	Ear, face, neck	0.5	0.8	0.003 (a)	0.3	1.5	1.8
745-747	Heart and circulatory system	7.9	4.3	5.0	3.6	8.4	10.5
748	Respiratory system	0.3	0.2	0.0 (a)	0.1	1.7	1.5
749	Cleft palate and cleft lip	1.5	1.8	1.5	1.5	1.8	1.7
750-751	Other parts of digestive system	2.8	1.8	2.6	0.5	3.8	6.3
752-753	Urogenital system	9.1	2.8	1.9	1.1	8.5	9
754-756	Musculoskeletal system	31.3 (b)	6.6	10.7	4.8	12.3	17.4
757	Integument	0.7	0.2	0.07 (a)	0.4	1.6	2.4
758	Chromosomal anomalies	1.3	1.4	1.9	1.2	1.3	1.3
759	Other	2.0	0.2	0.2	0.3	0.6	0.9
740-759	**Total**	59.7	22.2 44.8 (c)	25.1	16.2*	42.7*	52.8*
550	Inguinal hernia	11.0	0.1	6.2	0.02*	2.1*	7.9*
553	Umbilical hernia	0.9	0.3	-- --	-- --	-- --	-- --
227-228 (ICD8)	Congenital tumors	0.1	1.0	-- --	-- --	-- --	-- --
	Grand Total	71.7	23.6 46.2 (c)	31.3	16.2*	44.8*	60.7*

Footnotes:
(a) The present compilation does not include any cases attributed to multifactorial etiology under these ICD numbers, whereas appreciable numbers were attributed to a multifactorial etiology in the previous analysis of B.C. data.
(b) Incidence would be 5.5 if congenital dislocation of the hip were excluded.
(c) Adjusted for underestimation.
(d) Most of these rates are based on total diagnoses, and therefore have been adjusted downward by a factor of 0.8 (see main text). figures marked with * are based on actual cases and have not been adjusted.

Table 8.2

Incidence of genetic or partially-genetic diseases per 1000 live-births according to various reports

Disease category	B.C. 1964-69		B.C. 1952-83	UNSCEAR Reports			
	Minimal	Adjusted	sum of highest rates	1966	1977*	1982	1986
Dominant	0.6	0.8	1.4	10.0	10.0	10.0	10.0
X-linked	0.3	0.4	0.5				
Recessive	0.9	1.1	1.7	2.0	1.1	2.5	2.5
Chromosomal							
- numerical	1.6	2.0	1.9	4.0	4.0	4.0	3.4
- structural							0.4
Multifactorial							
- congenital	36.0	43.0	23.1	25.0	90.0	90.0	90.0
- other	16.0	47.0	23.9	15.0			
Genetic Unknown			1.2				
All	55.0	94.0	53.7	56.0	105.0	107.0	108.0

*The values used in the report of the BEIR committee in 1980 (8) were essentially identical to those in the 1977 UNSCEAR report.

Table 8.3

Evolution of estimates of contribution of various categories of genetic or partially-genetic diseases to the estimated total increase in incidence of these diseases after exposure of parents to low levels of radiation

	First generation only			Total summed over all generations		
	UNSCEAR 1977	BEIR 1980	UNSCEAR 1986	UNSCEAR 1977	BEIR 1980	UNSCEAR 1986
Increase per 1000 live-births per Sv	2-6	0.5 - 7.5	2.2	18.5	6 - 110	15
Relative Contribution						
Dominant & X-linked	91-32%	100-87%	68%	54%	67-22%	67%
Recessive	~ 0	~ 0	~ 0	S*	S*	S*
Chromosomal	9-60%	0-13%		22%	small	
- numerical			~ 0			~ 0
- structural			12%			3%
Multifactorial	0-8%	?	20%	24%	33-78%	30%

*Increase in recessive diseases over many generations is indicated only as being very slow (S).

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(See pages 543 and 546, Tables 45, 53 and 54, for mortality to age 5, rates of hospital admission, and numbers of days hospital stay for selected kinds of hereditary disorders, based on the Trimble and Smith data from British Columbia; also pages 544-545, Tables 46-50, for estimates of the birth frequencies, degrees of impairment, and lost years of life, for the various categories of genetic disease, based on the data of C.O. Carter.)

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APPENDIX 1

Table A1.1 Sources of data (from 1981 Annual Report)

Table A1.2 Types of data (from 1981 Annual Report)

Table A1.3 Example of early registration card

Table A1.4 First computer entry form

Table A1.5 Current computer entry form

Table A1.6 Etiology codes

Table A1.7 "Special" ICD codes

Table A1.8 Current recording instructions

Table A1.9 Record layout

Table A1.1
Number of cases reported in 1981 according to registering agency and other sources
(Comments on next page)

	Number of Cases
AGENCIES	
Vancouver Metropolitan Board of Health	188
Capital Regional District Community Health Services	60
Provincial Health Districts	1,128
Community Vocational Rehabilitation Services	999
Pacific Regional Medical Services (Federal Government)	228
Ministry of Human Resources Health Division	2,276
The Woodlands & Tranquille Schools and Glendale Lodge (Facilities for mentally retarded)	309
Vancouver General Hospital Health Centre for Children	157
Children's Hospital & Diagnostic Centre	3
G.F. Strong Rehabilitation Centre	344
Sunny Hill Hospital (Pediatric long-term-care hospital)	10
Cystic Fibrosis Clinic	21
Canadian Arthritis & Rheumatism Society	331
Canadian National Institute for the Blind	1,092
Lower Fraser Valley Cerebral Palsy Association	49
Multiple Sclerosis Association and Clinics (Victoria and Vancouver)	450
U.B.C. Genetics Clinics	354
Out-of-Province Genetic Clinics (mainly Calgary, Alberta)	13
Private Physicians	5
Chromosome Laboratories	355
Sub-Total	9,076
VITAL AND HOSPITAL RECORDS	
Physician's Notice of Birth	932
B.C. Hospitals Programs' Admission/Separation Form	5,767
Obstetrical Discharge Summary Form (an old system, phased out by 1985)	114
Stillbirth Registrations	264
Death Registrations	120
Sub-Total	7,197
GRAND TOTAL	16,273

Comments:

This table shows the total number of case reports that were received by the Registry from all sources of ascertainment during 1981.

Note that the numbers in these tables represent the total number of case-reports supplied to the Health Surveillance Registry during the year. They do not reflect the number of new or old cases. Thus, an individual new case may be reported more than once by different agencies in the first year, and additional case-reports for this same individual may well be supplied in subsequent years, allowing for updating of the record.

Acquisition of additional sources of reports is actively pursued. Thus, new reporting sources in 1981 were the Multiple Sclerosis Society of Victoria and Vancouver Island, the Cancer Control Agency of B.C., Holy Family Hospital, and the Hyperphenylalaninemia Clinics in Vancouver, Victoria and Woodlands (New Westminster). The Hyperphenylalaninemia Clinics support a risk subfile within the Registry of PKU cases that will require subsequent follow up.

(From the 1981 HSR Annual Report).

Table A1.2
Number of reports received during 1981 of (a) new cases (b) follow-up reports on cases previously reported

Reporting Agencies	Total Number of Reports Received	(a) New Cases		(b) Known Cases	
Government Agencies; Health Districts Community Vocational Rehabilitation Services Ministry of Human Resources, etc	5,235	3,154	(60%)	2,081	(40%)
Hospitals, treatment and Rehabilitation centres	2,294	1,342	(59%)	952	(41%)
Voluntary Agencies	1,176	655	(56%)	521	(44%)
Physicians	371	232	(63%)	139	(37%)
Vital and Hospital Records of congenital anomalies	7,197	3,915	(54%)	3,282	(46%)
All Agencies	16,273	9,298	(57%)	6,975	(43%)

Comments:

This table shows the number of reports received from the main groups of reporting agencies; i.e., government agencies, hospital and rehabilitation centres, voluntary agencies, physicians, and vital and hospital records. These figures are divided into the number of reports of new cases and of duplicate or follow-up reports received on cases already on the Registry's file. For example, 60 percent of cases reported by government agencies in 1981 were new cases, while the remaining 40 percent had been reported previously. The information on a single case contained in reports from several sources serves to add, up-date or correct the existing information, thus improving its accuracy and relevance.

The concept of building case histories through data from multiple reporting sources over an extended period of time is an integral part of the mechanism of the Health Surveillance Registry. More than one-third of the reports received by the Registry refer to existing cases on file. As the Registry has now been in existence for thirty years, the records may extend over the lifetime of some patients. Often data concerning second generations and other relatives are also available.

(From the 1981 HSR Annual Report).

TABLE A1.3

Example of early registration card.

DEPARTMENT OF HEALTH AND WELFARE. HEALTH BRANCH

Registry for Handicapped Children
828 W 10th Ave., Vancouver 9, B. C.

009545

DEAD

Surname DOE Christian Names JAMES Date of Birth March 6/57

Address 123 MAIN ST, KINGSTON, B. C. 840-44-39 Sex: Male ☐ Female ☒

Name of Parents or Guardian David and Mary DOE No. of children in family 1

DIAGNOSIS: (Disabilities - state degree - slight, moderate or severe) 7421(1) 315.2(2) 343.9(3)

(1) Microcephalic, (2) PROFOUND-MENTAL RETARDATION, (3) CEREBRAL PALSY

VISION ?

Is there any degree of Mental Retardation No ☐ Yes ☒ I.Q. ____

Does this child because of disability require any of the following:- Check items which apply.

1. Medical Investigation and/or Treatment ☐
2. Physical Rehabilitation ☐
3. Prolonged Institutional Care - Physical ☐
4. Institutional Care - Mental ☐
5. Special Educational Facilities ☐
6. Vocational Training ☐

Name, Position, Address of Person Registering:-

Division of Vital Statistics Registration Number 1234567 Date April 18/57

ARE YOU REGISTERING THIS CASE FOR:- Statistics ☐ Advice ☐ Active Follow-up ☐ If advice or follow-up, please complete rest of card.

Is family eligible for-
Hospital Outpatient Service ☐
Social Assistance ☐
Indian Health Services ☐

Names of Hospitals or Travelling Clinics attended with dates.
Grace Hospital, Vancouver, B. C. 10H
Died Nov. 30/57 V.S.# 015172

Occupation of Father and/or Mother
Logger

Name and Address of Family Physician
Dr. Jones, E.B.,
Grace Hospital,
Vancouver, B. C.

With the exception of Vancouver, please return all cards through the Local Health Unit Director
Form C.C. 1

64

(over)

Example of early registration card (continued)

School

Provincial
Family Number

Further Comments:-

AUG 9 1957 - C.C. 3 ret'd. Sept. 3/57 - Child under care of Dr. Smith ..., disability still present, not improved, any other defects? vision??? no assistance from Registry.

"This child is under Dr. Smith - the parents have entered the name to Woodlands School and are waiting for admission.

Aug. 13/59 - Additional regis. dated May 26/59 received from The Woodlands School for statistics.

Dec. 20/65 - R.3 rec'd. from Burnaby stating: Death and Cause: "Died Nov. 30/65 - Cause- Bronchopneumonia. Cerebral Palsy. Profound mental retardation."

Dec. 16/65 - On list from Woodlands and Dept
Sources 64, 55
Woodlands. Nov/29
Hc. May 1/61, age 4yrs 1 mo, 2wks. 16½"

Registry for Handicapped Children
RECEIVED
APR 23 1957
VANCOUVER, B.C.

Birthplace
Birth No.
Etiology
Family
Age at Regis.
Inst. or son H
Age at Death

TABLE A1.4

First computer entry form

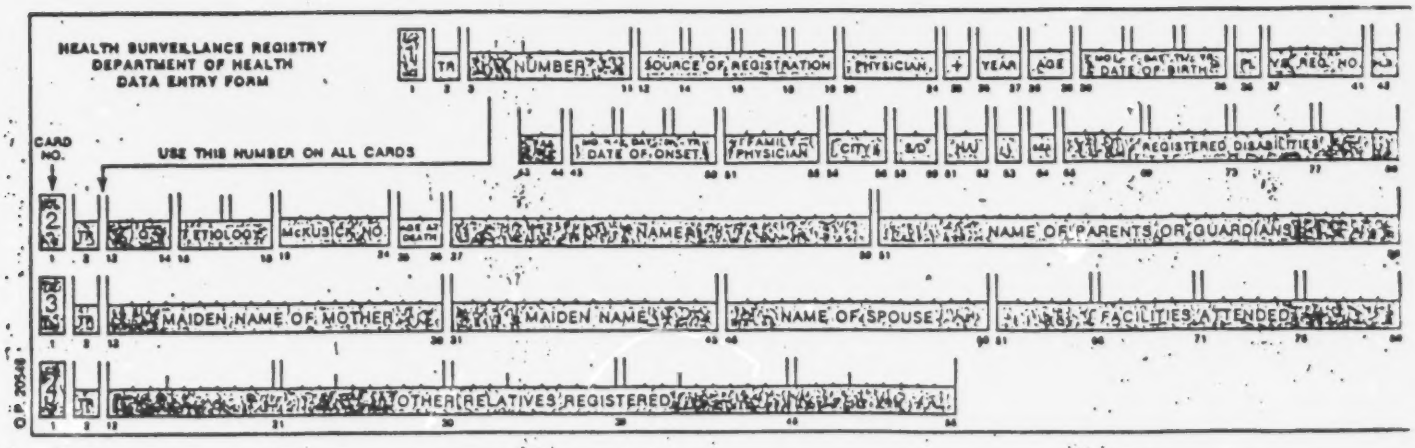

Table A 1.4 Original coding sheet, in use from 1974 until December 1982. Since January 1, 1983, computer data entry has been done directly from the record card shown in Table 2.5.

TABLE A 1.5

Current computer entry form

Province of British Columbia — Ministry of Health

HEALTH SURVEILLANCE REGISTRY
828 WEST 10th AVENUE, VANCOUVER, B.C. V5Z 1L8

1

2

3 SURNAME | 4 GIVEN NAMES | 5 BIRTH DATE (Y/M/D)

6 ADDRESS | 7. REG. | 8. CUR.

9 SEX M F | 10 BIRTH SINGLE OR MULTIPLE SGL TWN TRI OTH | 11 CITY AND/OR COUNTRY OF BIRTH | 12. PL | 13. V.S. REG. NUMBER

14 ETHNIC ORIGIN IF KNOWN | 15 BIRTH SURNAME IF DIFFERENT FROM ABOVE | 16 OTHER RELATIVES REGISTERED | 17. CURRENT PARTNER'S NAME

18 PARENT'S/GUARDIAN'S NAMES | 19 MOTHER'S BIRTH SURNAME

20 HOSPITALS ATTENDED

21 FAMILY PHYSICIAN | 22 DATE OF DEATH (Y/M/D) | 23 DEATH REG. No. | CAUSE OF DEATH 24.1 24.2

25. SOURCE NUMBERS

REGISTERED BY

(FH 1141 (REV. 83/01))

Layout of first "page" of the Registration card used since January 1983 — for new births and for updating of previously registered cases.

Reverse of card is shown on next 2 pages.
Note: card is approximately 24 cm x 20 cm, with the top half of this first side being blank, and available for notes. Card is folded — creating 4 "pages".

Table A1.5
(continued)

Current computer entry form (continued)

ETIOLOGY: INDICATE ANY CLUES AS TO THE CAUSE OF THIS CONDITION, SUCH AS MATERNAL INFECTION, BIRTH TRAUMA, HEREDITARY, POST NATAL TRAUMA OR INFECTION (E.G. MENENGITIS) ETC

26. DATE REPORTED	27. DIAGNOSIS/DISABILITIES (ONE PER ENTRY LINE)	28. ICD9	29. DATE OF ONSET OR DIAGNOSIS (Y/M/D)	30. E.T.	31. McKUSICK #	32. FUNCTIONAL LEVEL

Table A1.5
(continued)

Current computer entry form (continued)

COMMENTS INDICATE ANY SOCIAL OR EMOTIONAL PROBLEMS IN PATIENT AND/OR FAMILY WHO ARE HANDICAPPED ETC

33 NAME	34 RELATIONSHIP	35 CASE NUMBER	33 NAME	34 RELATIONSHIP	35 CASE NUMBER

TABLE A 1.6

Etiology codes used in conjunction with ICD codes by the Health Surveillance Registry.

00	Not Known
01	Genetic - Unspecified
02	Genetic - Dominant
03	Genetic - Recessive
04	Genetic - X-Linked
05	Genetic - Chromosome - Autosome (Down Syndrome)
06	Genetic - Chromosome - Sex
07	Multifactorial (polygenic) Inheritance
11	Prenatal Environmental Factors - Trauma, NOS
12	Prenatal Environmental Factors - Maternal Ingestion of drugs not classifiable by specific etiology code, or unspecified.
13	Prenatal Non-viral Infection, other and unspecified
14	Prenatal incompatibility of antigenic factors between mother and baby (e.g. RH incompatibility).
15	Prenatal Environmental Factors - Radiation NOS
16	Prenatal Environmental Factors - Anoxia and Asphyxia
17	Prenatal Environmental Factors - Other (e.g. maternal diabetes)
21	Congenital - present at beginning of birth process.
31	Birth Trauma - Asphyxia and Anoxia
32	Birth Trauma - Unspecified
39	Cerebral Palsy (343 - excluding 343.7) (under 2 yrs of age)
41	New Growths (Cancer) - Birth to 18 years.
51	Infections
60	Trauma Unspecified
61	Child Battering
62	Trauma, Burns
63	Late Effects of Poison, Drugs, Alcohol, etc.
64	Trauma - Asphyxia (Drowning, smothering)
65	Therapeutic Procedure, e.g. High O_2
66	Degenerative Condition Associated with Age
71	Nutritional
75	Psycho-social Deprivation
80	Prenatal - Maternal Alcoholism
81	Prenatal - Maternal Ingestion of Hydantoins
90	Prenatal - Rubella Infection
91	Prenatal - Viral Infections other than Rubella

TABLE A 1.7

"Special" Diagnostic Codes used by the Health Surveillance Registry

(Registry codes not found in the ICD 9th revision and ICD 9th revision codes with a different diagnostic classification in the Registry)

1) Special Registry Codes, Not in ICD 9th Revision

Special Registry Code	Classification and Remarks
317.1	Borderline mental retardation (I.Q. 70 to 95)
317.2	Mild mental retardation-equivalent to 3-digit ICD category 317. (I.Q. 50 to 70)
340.0	Multiple sclerosis, confirmed
340.1	probable multiple sclerosis
340.2	possible multiple sclerosis
343.5	Athetoid cerebral palsy (athetoid, athetosis, chorioatheoid, chorioathetosis, athetoid movements). Exclude Vogt's Disease (ICD code 333.7) if so stated.
343.7	Minimal cerebral dysfunction
379.6	Disorders of lens excluding aphakia (e.g. dislocation, subluxation)
754.9	Dislocatable hip Unstable hip Subluxatable hip Hip click Loose lax hip Note that the above diagnoses denoted by code 754.9 are excluded from ICD code 754.3 for congenital dislocation of hip.

Note: Any Registry code ending with an X in the 4th digit position is equivalent to the corresponding 3-digit ICD category (i.e. where there is no 4th digit sub-classification). For example, ICD code 319 for unspecified mental retardation is recorded as 319X.

Table A1.7
(continued)

"Special" Diagnostic Codes used by the Health Surveillance Registry (continued)

2) ICD 9th Revision Codes With a Different Meaning in the Registry

ICD CODES	ICD CLASSIFICATION	REGISTRY CLASSIFICATION
228.0	Hemangioma, any site	Hemangioma of sites other than skin.
250.0	Diabetes mellitus without mention of complication	Adult onset diabetes mellitus
250.1	Diabetes with ketoacidosis	Juvenile onset diabetes mellitus
270.2	Other disturbances of aromatic amino-acid metabolism - a catchall category including ocular albinism which is coded to both 270.2 and 743.8 in the ICD system	Same, but excluding ocular albinism which is coded to 743.8 only.
333.7	Symptomatic torsion dystonia ICD inclusion worded as follows: athetoid cerebral palsy or Vogt's disease; double athetosis.	Vogt's disease or double athetosis only - excludes diagnoses shown under special Registry code 343.5.
345.7	Epilepsia partialis continua (Kojevnikov's epilepsy).	Mixed epilepsy (combination of Grand Mal & Petit Mal).
345.8	Other epilepsy - a catchall group excluding epilepsia partialis continua.	Other epilepsy - a catchall including epilepsia partialis continua.
345.9	Unspecified epilepsy - excludes febrile convulsions (code 780.3).	Unspecified epilepsy - includes febrile convulsions.
358.8	Other myoneural disorders - a catchall category excluding congenital hypotonia, not stated as benign (code 779.8)	Same, but including congenital hypotonia not stated as benign.
378.0	Convergent con-comitant strabismus (specific 4-digit code in ICD category 378).	Strabismus and other disorders of binocular eye movements (heading in ICD for 3-digit category 378). In the Registry system code 378.0 is equivalent to ICD category 378, excl. 378.'
379.3	Aphakia and other disorders of lens	Aphakia (specifically)
389.8	Catchall category designated "other specified forms of deafness".	Deafness in one ear only.

"Special" Diagnostic Codes used by the Health Surveillance Registry (continued)

ICD CODES	ICD CLASSIFICATION	REGISTRY CLASSIFICATION
743.8	Other specified anomalies of eye a catchall category including ocular albinism which is coded to 270.2 as well as 743.8 in the ICD system.	Same, but ocular albinism is coded to 743.8 only
752.8	Other specified anomalies of genital organs - a catchall category excluding congenital hydrocele (code 778.6).	Includes congenital hydrocele.
754.3	Congenital dislocation of hip- classification includes the following additional terms: Congenital: dislocatable hip preluxation hip Predislocation status of hip at birth.	Congenital dislocation of hip - classification includes the additional terms: acetabular hypoplasia acetabular dysplasia subluxated hip Excludes: dislocatable hip, etc. (See special Registry code 754.9).
754.7	Other deformities of feet - a catchall category excluding varus deformities (code 754.5) and valgus deformities (code 754.6).	Clubfoot (congenital); equivalent to ICD codes 754.5, 754.6 & 754.7, i.e. varus, valgus & other deformities of feet.
755.1	Syndactyly - excludes acrocephalosyndactyly (code 755.5).	Syndactyly - includes acrocephalosyndactyly which is always assigned both codes 756.0 & 755.1 in the Registry system.
755.5	Other anomalies of upper limb, including shoulder girdle - a catchall category including acrocephalosyndactyly.	Same, but excluding acrocephalosyndactyly (see 755.1 and 756.0 under Registry classification).
756.0	Anomalies of skull and face bones - a catchall category excluding acrocephalo-syndactyly (code 755.5)	Same, but including acrocephalo-syndactyly which is always assigned both codes 756.0 & 755.1 in the Registry system.
756.7	Anomalies of abdominal wall - excludes omphalocele (code 553.1); includes congenital diastasis recti.	Anomalies of abdominal wall - includes omphalocele excludes congenital diastasis recti (code 728.8).

"Special" Diagnostic Codes used by the Health Surveillance Registry (continued)

ICD CODES	ICD CLASSIFICATION	REGISTRY CLASSIFICATION
756.7	Anomalies of abdominal wall- excludes omphalocele (code 553.1); includes congenital diastasis recti	Anomalies of abdominal wall- includes omphalocele: excludes congenital diastasis recti (code 728.8).
757.3	Other specified anomalies of skin - a catchall category excluding hemangioma (code 228.0)	Same, but including hemangioma of skin, and hemangioma not otherwise specified.
762.8	Other abnormalities of chorion and amnion - a catchall category under the 3-digit category of 762 designating "Fetus or newborn affected by complications of placenta, cord and membranes".	Amniotic Constriction Band Syndrome (code used for this condition only)

TABLE A1.8

Current recoding instructions

PURPOSE:

To register children and adults who have birth, genetic or chronic disabilities with the Health Surveillance Registry (H.S.R.) so that a record of the frequency and distribution of these conditions in the British Columbia population is available.

PROCEDURE:

Use the following instructions to fill in data on the registration form as completely as possible; however, the form can be submitted with partial information:

The minimum information that is required for registration is:

Surname
Year of Birth
Sex
One diagnosis or disability
Reporting Source (agency or institution)
Name of parent or guardian (if a child)

RECORDING:

Please type or print information clearly. Do not write in the green shaded areas as these are for H.S.R. use only.

Enter all dates as year/month/day, e.g. 1983/01/01 or 1983,Jan. 01

If extra space is needed for subjective information, please use "comments" section. The back of the card may also be used, if necessary.

Front of Form

3. *Surname: Print name legibly.*
4. *Given Names: Include all given names if known as this is sometimes necessary for identification.*
5. *Birth Date: Use year/month/date format.*
6. *Address: Use full address including postal code. Use only one line so that the extra lines can be used for address changes.*
9. *Sex: Enter "√" in the appropriate box.*
10. *Birth Single or Multiple: Check "√" SGL if a single birth.*
    If a multiple birth, indicate birth order, i.e.
    TWI - Twin, fill in "A" or "B"
    TRI - Triplet, fill in "A", "B" or "C"
    OTH - Other, fill in "A", "B", "C", "D" or "E", etc.

B.C. Ministry of Health

March, 1983

Current recoding instructions (continued)

11. City and/or Country of Birth: Show city/town and province, or country if outside Canada.

14. Ethnic Origin if Known: Enter the race of the individual, i.e. Native Indian, Chinese, etc.

15. Birth Surname if Different From Above: If a married woman, enter her maiden name. If an adopted or foster child and the birth surname is known, please enter it in this space.

16. Other Relatives Registered: Please leave blank. This space is for H.S.R. only.

17. Current Partner's Name: Enter the given names of spouse and also surname if different; enter full name of common-law partner.

18. Parents'/Guardians' Names: Enter the given names of each parent, if known, or the full names of foster parents or guardians. Please indicate adoptive parents by A/P or foster parents by F/P.

19. Mother's Birth Surname: Enter mother's maiden name.

20. Hospitals Attended: Enter the name of hospital or community health centre where the person was treated.

21. Family Physician: Enter the name of the family doctor or specialist, if family doctor is not known.

Registered By: Enter the name of the registering source and the date, e.g. Skeena Health Unit, 1983, March 8 (Y/M/D).

Inside Upper Section of Form.

Etiology: Indicate any clues as to the cause of this condition, such as maternal infection, birth trauma, heredity, postnatal trauma, infection (e.g. Meningitis), motor vehicle accident, etc.

27. Diagnosis/Disabilities (One Per Entry Line): Enter one registrable condition on each line. This may be a

(a) medical diagnosis e.g., cleft lip/palate, diabetes mellitus Down Syndrome, etc. or a

(b) disability (*any restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human being) such as speech problem, visual loss, amputations or a manifestation of health problems such as hypotonia, muscle wasting or atrophy, late effects of spinal cord injury, etc.

* World Health Organization, International Classification of Impairments, Disabilities, and Handicaps. Geneva, 1980.

Current recoding instructions (continued)

29. *Date of Onset or Diagnosis (Y/M/D): Enter date of onset or diagnosis for each condition if known. If both dates are known enter the date of onset. Use Year/Month/Day format if known, otherwise use Year/Month or Year, e.g. Down Syndrome,1982/01/18.*

Lower Section of Form

Comments: Indicate any social or emotional problems in patient and/or family who are handicapped;

and if possible, the level or amount of disability, i.e. wheelchair, special class at school, etc.

If registering a disorder present at birth, indicate any medication or other drugs taken by the mother during pregnancy e.g. medication to control epilepsy, abuse of alcohol, exposure to toxic substances, etc. Also indicate if mother has a chronic disorder, e.g. diabetes mellitus, epilepsy, hyperphenylalaninemia, etc.

B.C. Ministry of Health
March, 1983

TABLE A1.9

Record Layout

RECORD LAYOUT FOR NEW HEALTH SURVEILLANCE REGISTRY SYSTEM

SEGMENT	FIELD POSITION	FIELD NUMBER	FIELD SIZE	FIELD DESCRIPTION
A) IDENTIFICATION				
	1-6	1	6	Case Number
	7-30	2	24	Name
	31-38	3	8	Birthdate YYYYMMDD
	39	4	1	Sex 1-Male 2-Female 3-Unknown 4-Misidentified
	40-47	5	8	Registration Date YYYYMMDD
	48-55	6	8	Bring Forward Date YYYYMMDD
	56-62	7	7	Current Address Code City (3) School Districts (2) Health Unit (2)
	63-69	8	7	Address Code at Time of Registration City (3) School District (2) Health Unit (2)
	70	9	1	Location Code at Time of Birth 0 - Birthplace Unknown 1 - Birth in B.C. - 1952 or later 2 - Birth outside B.C. - 1952 or later 3 - Birth In or Outside B.C. - before 1952 8 - Stillbirth in B.C.
	71	10	1	Multiple Y or N
	72-76	11	5	Vital Statistics Registration
	77-126	12	50	Name of Parents
	127-145	13	19	Birth Surname of Mother
	146-164	14	19	Birth Surname (Maiden Name of Married Women)
	165-188	15	24	Name of Current Partner (Spouse)
	189-193	16	5	Cause of Death1 (ICD9)
	194-198	17	5	Cause of Death2 (ICD9)
	199-206	18	8	Date of Death
	207-211	19	5	Family Physician (Code)
	212-214	20	3	Ethnic Race of Origin (Code)

Record Layout (continued)

SEGMENT	FIELD POSITION	FIELD NUMBER	FIELD SIZE	FIELD DESCRIPTION
A) IDENTIFICATION (cont'd)				
	215	21	1	Other Relatives Registered Y or N
	216-220	22	5	Hospital Facility Attended1 (Code)
	221-225	23	5	Hospital Facility Attended2 (Code)
	226-230	24	5	Hospital Facility Attended3 (Code)
	231-235	25	5	Hospital Facility Attended4 (Code)
	236-240	26	5	Hospital Facility Attended5 (Code)
	241-245	27	5	Hospital Facility Attended6 (Code)
	246-247	28	2 (Binary)	Occurance Counter for Source Segments
	248-249	29	2 (Binary)	Occurance Counter for Diagnosis Segments
B) SOURCE OF REGISTRATION (Maximum 12 Segments per Case)				
		1	3	Source of Registration (Code)
C) DIAGNOSIS (Maximum 20 Segments per Case)				
	1-5	1	5	ICD9 Code
	6-13	2	8	Date of Registration for a Given Diagnosis
	14-21	3	8	Date of Onset of Diagnosis
	22-23	4	2	Etiology Code
	24-29	5	6	McKusick Code

APPENDIX 2

Table A2.1 Example of worksheets.

Table A2.2 Complete tabulation of dominant conditions by birth-year ranges.

Table A2.3 Complete tablulation of recessive conditions by birth-year ranges.

Table A2.4 Complete tabulation of X-linked conditions by birth ranges.

TABLE A2.1

Illustration of procedure used to resolve ambiguous cases

(Example of raw data on next page.)

WORKSHEET -- McKUSICK-ICD CONSISTENCY -- DOMINANTS

The intention here is to create a list of McKusick numbers showing:

a) how many cases there are for each,
b) how many times the various ICD numbers are assigned to each, and
c) where the cases are to be found

The suggestion will then be made that, for a given McKusick number, always the same ICD number be assigned to represent that McKusick number. This way, all cases with a given McKusick number can be made to fall together consistently into a single group. One has simply to designate the ICD code associated with a McKusick number as the one to be used for sequencing the records that have a McKusick number. This does not solve the problem of fragmented groupings where there is no McKusick number, but it does set a pattern that might help there as well.

	Page no	Prin ICD list	McK and [no of cases]	ICD and [no of cases]	Other ICDs and [nos of cases]		Suggested ICD for grouping
ok	61-69	7564	10080[20]	7564[20]	7371, 7423	ACHONDROPLASIA	756.4 (ICD index p 15)
x	77	7568	10080[1]	7568[1]	7483, 7538, 7553	ACHONDROPLASIA	
x	42	7422	10120[1]	7422[1]	none	ACROCEPHALOSYNDACTYLY (APERT	755.5 (ICD index p 16 + p 478)
x	54	7552	10120[1]	7551[1]	3795, 7502, 7560, 7576	ACROCEPHALOSYNDAC (APER	
ok	56	7555	10120[1]	7555[1]	none	ACROCEPHALOSYNDACTYLY (APERT	
x	58-60	7560	10120[3]	7560[3]	7422, 7490, 7551[2]	ACROCEPHALOSYNDACTYLY (APE	
x	60	7560	10160[1]	7560[1]	7431, 7551	ACROCEPHALOSYNDACTYLY (PFEIF	
	92	7598	10420[2]	7598[2]	3891[2], 7533[2]	HERED NEUROP & DEAFN (ALPORT	
	41	5205	10450[2]	5205[2]	none	AMELOGENESIS IMPERFECTA	
	27	3352	10540[1]	3352[1]	none	LATERAL SCLEROSIS, AMYOTROPH	
	46-47	7434	10620[8]	7434[8]	3659, 3669, 3671, 3690[7], 3699, 3706. 3795[6], 7431, 7433	ANIRIDIA	
	24	2865	10730[1]	2865[1]	none	ANTITHROMBIN III DEFICIENCY	
	15	2776	10740[3]	2776[3]	none	ANTITRYPSIN	
	57	7558	10812[2]	7558[2]	none	ARTHROGRYPOSIS MULTIPLEX	
	35	3627	10830[1]	3627[1]	7138	ARTHROOPHTHALMOPATHY (STICKL	

DOMINANT)	CASE-NO	SEX	B.YR	PRDIAG		CODE-1	CODE-2	CODE-3	CODE-4	CODE-5	CODE-6	CODE-
	CHONDRODYSTROPHY (cont)											
716 ✓	256049	2	1970	7564	ICD :	(7564)	7369					
					ET :	02	02					
					MCK :	013370	013370 ✓					
717	121526	2	1972	7564	ICD :	7564						
					ET :	02						
					MCK :	012782 ✓						
718	250276	1	1972	7564	ICD :	7564						
					ET :	02						
					MCK :							
719	251646	2	1972	7564	ICD :	7564						
					ET :	02						
					MCK :							
720	101381	2	1973	7564	ICD :	7564	7527					
					ET :	02	21					
					MCK :							
721	306085	1	1974	7564	ICD :	7564						
					ET :	02						
					MCK :							
722 ✓	259950	1	1975	7564	ICD :	(7564)	7423	7454				
					ET :	02	02	07				
					MCK :							
723	265937	1	1976	7564	ICD :	7564						
					ET :	02						
					MCK :							
724 ✓	273643	1	1977	7564	ICD :	(7564)	7560	7485				
					ET :	02	02	02				
					MCK :							
725 ✓	122672	2	1978	7564	ICD :	7564	7455					
					ET :	02	07					
					MCK :	010080 ✓						
726 ✓	279112	1	1979	7564	ICD :	(7564)	7423	4939	7371			
					ET :	02	02	00	02			
					MCK :	010080	010080 ✓		010080 ✓			

Table A2.1
(continued)

Table A 2.2

Complete tabulation of dominant conditions by birth-year ranges

ICD9	DOMINANT CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
190.5	Retina, Malignant Neoplasm	6	13.7	14	40.6	16	41.3	36	30.8
211.3	Colon, Benign Neoplasm	1	2.3	0	0.0	0	0.0	1	0.9
237.7	Neurofibromatosis	34	77.7	33	95.7	32	82.5	99	84.6
252.1	Hypoparathyroidism	0	0.0	1	2.9	0	0.0	1	0.9
272.2	Mixed Hyperlipidaemia	1	2.3	0	0.0	0	0.0	1	0.9
272.4	Other and Unspecified Hyperlipidaemia	0	0.0	1	2.9	0	0.0	1	0.9
275.3	Disorders of Phosphorus Metabolism	3	6.9	1	2.9	1	2.6	5	4.3
275.4	Disorders of Calcium Metabolism	0	0.0	0	0.0	1	2.6	1	0.9
276.8	Hypopotassaemia	1	2.3	0	0.0	0	0.0	1	0.9
277.1	Disorders of Porphyrin Metabolism	1	2.3	1	2.9	0	0.0	2	1.7
277.4	Disorders of Bilirubin Excretion	1	2.3	0	0.0	0	0.0	1	0.9
277.6	Other Deficiences of Circulating Enzymes	0	0.0	0	0.0	4	10.3	4	3.4
277.8	Other Disorders of Metabolism	1	2.3	7	20.3	11	28.4	19	16.2
282.0	Hereditary Spherocytosis	12	27.4	18	52.2	20	51.6	50	42.7
282.1	Hereditary Elliptocytosis	0	0.0	0	0.0	2	5.2	2	1.7
282.4	Thalassaemias	0	0.0	4	11.6	4	10.3	8	6.8
282.5	Sickle-Cell Trait	0	0.0	0	0.0	1	2.6	1	0.9
286.0	Congenital Factor VIII Disorder	0	0.0	3	8.7	0	0.0	3	2.6
286.4	Von Willebrand's Disease	5	11.4	7	20.3	8	20.6	20	17.1
286.5	Haemorrhagic Dis Due to Circ Anticoagulants	0	0.0	1	2.9	0	0.0	1	0.9
287.3	Primary Thrombocytopenta	3	6.9	1	2.9	2	5.2	6	5.1
289.8	Other Disease of Blood	0	0.0	2	5.8	0	0.0	2	1.7
319.0	Unspecified Mental Retardation	1	2.3	1	2.9	1	2.6	3	2.6
333.0	Other Degen Diseases of the Basal Ganglia	3	6.9	0	0.0	0	0.0	3	2.6
333.1	Essential and Other Spec Forms of Tremor	1	2.3	0	0.0	0	0.0	1	0.9

Table A 2.2

Dominant conditions .....continued

ICD9	DOMINANT CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
333.2	Myoclonus	2	4.6	0	0.0	0	0.0	2	1.7
333.4	Huntington's Chorea	7	16.0	0	0.0	0	0.0	7	6.0
333.6	Idiopathic Torsion Dystonia	1	2.3	1	2.9	0	0.0	2	1.7
334.1	Hereditary Spastic Paragplegia	1	2.3	0	0.0	0	0.0	1	0.9
334.2	Primary Cerebellar Degeneration	1	2.3	2	5.8	1	2.6	4	3.4
334.3	Other Cerebellar Ataxia	0	0.0	4	11.6	0	0.0	4	3.4
335.2	Motor Neurone Disease	1	2.3	0	0.0	0	0.0	1	0.9
337.9	Unspec Disorders of Autonomic Nervous System	2	4.6	1	2.9	3	7.7	6	5.1
343.1	Hemiplegic Infantile Cerebral Palsy	2	4.6	0	0.0	1	2.6	3	2.6
345.1	Generalized Convulsive Epilepsy	1	2.3	1	2.9	0	0.0	2	1.7
345.9	Unspecified Epilepsy	3	6.9	3	8.7	0	0.0	6	5.1
352.6	Multiple Cranial Nerve Palsies	6	13.7	1	2.9	1	2.6	8	6.8
354.5	Mononeuritis Multiplex	1	2.3	0	0.0	0	0.0	1	0.9
356.0	Hereditary Peripheral Neuropathy	1	2.3	0	0.0	0	0.0	1	0.9
356.1	Peroneal Muscular Atrophy	7	16.0	3	8.7	3	7.7	13	11.1
359.1	Hereditary Progressive Muscular Dystrophy	4	9.1	3	8.7	0	0.0	7	6.0
359.2	Myotonic Disorders	14	32.0	8	23.2	6	15.5	28	23.9
362.4	Separation of Retinal Layers	1	2.3	0	0.0	0	0.0	1	0.9
362.5	Degeneration of Macula and Posterior Pole	0	0.0	1	2.9	0	0.0	1	0.9
362.7	Hereditary Retinal Dystrophies	13	29.7	0	0.0	0	0.0	13	11.1
365.9	Unspecified Glaucoma	1	2.3	0	0.0	0	0.0	1	0.9
366.0	Infantile, Juvenile and Presenile Cataract	3	6.9	0	0.0	1	2.6	4	3.4
367.1	Myopia	1	2.3	1	2.9	1	2.6	3	2.6
369.0	Blindness, Both Eyes	1	2.3	0	0.0	1	2.6	2	1.7
371.5	Hereditary Corneal Dystrophies	0	0.0	1	2.9	2	5.2	3	2.6

Table A2.2
(continued)

Table A 2.2

Dominant conditions.....continued

*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD9	DOMINANT CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
377.1	Optic Atrophy	2	4.6	0	0.0	0	0.0	2	1.7
378.7	Other Strabismus	0	0.0	0	0.0	1	2.6	1	0.9
379.5	Nystagmus and Other Irregular Eye Movements	14	32.0	2	5.8	3	7.7	19	16.2
379.6*	Other Disorders of Lens	0	0.0	0	0.0	1	2.6	1	0.9
389.1	Sensorineural Deafness	3	6.9	15	43.5	4	10.3	22	18.8
389.9	Unspecified Deafness	2	4.6	1	2.9	0	0.0	3	2.6
520.0	Anodontia	0	0.0	1	2.9	0	0.0	1	0.9
520.5	Hereditary Disturbance in Tooth Structure (N.E.C.)	3	6.9	0	0.0	2	5.2	5	4.3
579.0	Coeliac Disease	0	0.0	2	5.8	0	0.0	2	1.7
709.0	Dyschromia	1	2.3	0	0.0	0	0.0	1	0.9
728.1	Muscular Calcification and Ossification	1	2.3	2	5.8	0	0.0	3	2.6
728.6	Contracture of Palmar Fascia	1	2.3	0	0.0	0	0.0	1	0.9
732.1	Juvenile Osteochondrosis of Hip and Pelvis	2	4.6	0	0.0	0	0.0	2	1.7
742.3	Congenital Hydrocephalus	0	0.0	1	2.9	0	0.0	1	0.9
742.4	Other Specified Anomalies of Brain	0	0.0	1	2.9	4	10.3	5	4.3
743.2	Buphthalmos	1	2.3	0	0.0	0	0.0	1	0.9
743.3	Congenital Cataract and Lens Anomalies	21	48.0	10	29.0	5	12.9	36	30.8
743.4	Coloboma & Other Anomalies of Anterior Segments	5	11.4	3	8.7	4	10.3	12	10.3
743.5	Congenital Anomalies of Posterior Segment	1	2.3	0	0.0	1	2.6	2	1.7
743.6	Congen Anom of Eyelids, Lacrimal System and Orbit	0	0.0	5	14.5	2	5.2	7	6.0
743.9	Unspecified Anomalies of Eye	0	0.0	0	0.0	1	2.6	1	0.9
744.2	Other Specified Anomalies of Ear	0	0.0	0	0.0	1	2.6	1	0.9
746.8	Other Specified Anomalies of Heart	1	2.3	0	0.0	0	0.0	1	0.9
747.0	Patent Ductus Arteriosus	0	0.0	0	0.0	1	2.6	1	0.9
749.2	Cleft Palate with Cleft Lip	0	0.0	3	8.7	1	2.6	4	3.4

Table A2.2 (continued)

Table A 2.2

Dominant conditions.....continued

*Indicates special Registry code (see Appendix 1, Table A 1.7)

ICD9	DOMINANT CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
752.4	Anom of Cervix, Vagina and Ext F Genitalia	0	0.0	0	0.0	1	2.6	1	0.9
752.6	Hypospadias and Epispadias	0	0.0	2	5.8	2	5.2	4	3.4
753.1	Cystic Kidney Disease	2	4.6	4	11.6	3	7.7	9	7.7
755.0	Polydactyly	6	13.7	16	46.4	14	36.1	36	30.8
755.1*	Syndactyly	0	0.0	1	2.9	4	10.3	5	4.3
755.2	Reduction Deformaties of Upper Limb	1	2.3	4	11.6	6	15.5	11	9.4
755.3	Reduction Deformaties of Lower Limb	1	2.3	1	2.9	0	0.0	2	1.7
755.5*	Other Anom of Upper Limb, Inc Shoulder Girdle	3	6.9	2	5.8	9	23.2	14	12.0
755.8	Other Specified Anomalies of Unspecified Limb	2	4.6	4	11.6	1	2.6	7	6.0
756.0*	Anomalies of Skull and Face Bones	9	20.6	11	31.9	14	36.1	34	29.1
756.1	Anomalies of Spine	6	13.7	3	8.7	1	2.6	10	8.5
756.4	Chondrodystrophy	48	109.7	21	60.9	20	51.6	89	76.1
756.5	Osteodystrophies	24	54.9	31	89.9	29	74.8	84	71.8
756.8	Other Spec Anom of Muscle, Tendon, Fascia, etc.	13	29.7	14	40.6	7	18.1	34	29.1
756.9	Unspecified Anomalies of Musculoskeletal System	2	4.6	8	23.2	0	0.0	10	8.5
757.0	Hereditary Oedema of Legs	0	0.0	0	0.0	2	5.2	2	1.7
757.1	Ichthyosis Congenita	0	0.0	1	2.9	3	7.7	4	3.4
757.3*	Other Specified Congenital Anomalies of Skin	11	25.1	5	14.5	6	15.5	22	18.8
759.5	Tuberous Sclerosis	13	29.7	23	66.7	22	56.7	58	49.6
759.6	Other Congenital Hamartoses (N.E.C.)	7	16.0	1	2.9	3	7.7	11	9.4
759.7	Multiple Congenital Anomalies, So Described	8	18.3	7	20.3	5	12.9	20	17.1
759.8	Other Specified Congenital Anomalies	17	38.9	16	46.4	9	23.2	42	35.9
781.0	Abnormal Involuntary Movements	0	0.0	0	0.0	1	2.6	1	0.9
TOTAL		379	866.3	346	1003.9	316	815.1	1041	889.8
SUM OF HIGHEST INDIVIDUAL RATES									1395.4

Table A2.2 (continued)

Table A 2.3

Complete tabulation of Recessive conditions by birth-year ranges

*Indicates special Registry code (Appendix 1, Table A 1.7)

ICD9	RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
202.5	Letterer-Siwe Disease	5	11.4	3	8.7	0	0.0	8	6.8
243	Congenital Hypothyroidism	1	2.3	2	5.8	0	0.0	3	2.6
251.8	Other Disorders of Pancreas	0	0.0	1	2.9	1	2.6	2	1.7
253.3	Pituitary Dwarfism	0	0.0	2	5.8	0	0.0	2	1.7
253.4	Other Anterior Pituitary Disorders	0	0.0	0	0.0	1	2.6	1	0.9
253.8	Other Disorders of Pituitary, etc	0	0.0	1	2.9	0	0.0	1	0.9
255.1	Hyperaldosteronism	13	29.7	7	20.3	1	2.6	21	18.0
255.2	Adrenogenital Disorders	5	11.4	8	23.2	12	31.0	25	21.4
266.1	Vitamin B6 Deficiency	0	0.0	0	0.0	2	5.2	2	1.7
270.0	Disturbances of Amino-Acid Transport	0	0.0	3	8.7	6	15.5	9	7.7
270.1	Phenylketonuria	26	59.4	18	52.2	31	80.0	75	64.1
270.2*	Other Disturbances of Aromatic AA Metabolism	22	50.3	19	55.1	16	41.3	57	48.7
270.3	Disturbances of Branched-Chain AA Metabolism	0	0.0	0	0.0	2	5.2	2	1.7
270.4	Disturbances of Sulphur-Bearing AA Metabolism	8	18.3	3	8.7	1	2.6	12	10.3
270.5	Disturbances of Histidine Metabolism	0	0.0	1	2.9	0	0.0	1	0.9
270.6	Disorders of Urea Cycle Metabolism	0	0.0	1	2.9	3	7.7	4	3.4
270.7	Other Disturb of Straight-Chain AA Metabolism	0	0.0	2	5.8	5	12.9	7	6.0
270.9	Unspecified Dis of AA Transport & Metabolism	0	0.0	0	0.0	1	2.6	1	0.9
271.0	Glycogenosis	3	6.9	12	34.8	8	20.6	23	19.7
271.1	Galactosaemia	3	6.9	4	11.6	5	12.9	12	10.3
271.2	Hereditary Fructose Intolerance	0	0.0	0	0.0	1	2.6	1	0.9
271.3	Intesti Disaccharidase Def & Malabsorption	0	0.0	1	2.9	6	15.5	7	6.0
271.8	Other Disorders of CHO Transport and Metabolism	1	2.3	0	0.0	0	0.0	1	0.9
271.9	Unspec. Disorders of CHO Transport & Metabolism	0	0.0	0	0.0	2	5.2	2	1.7
272.0	Pure Hypercholesterolaemia	0	0.0	0	0.0	1	2.6	1	0.9

Table A 2.3

Recessive conditions..... continued

ICD9	RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
272.3	Hyperchylomicronaemia	0	0.0	1	2.9	0	0.0	1	0.9
272.7	Lipidoses	4	9.1	10	29.0	4	10.3	18	15.4
275.1	Disorders of Copper Metabolism	1	2.3	1	2.9	0	0.0	2	1.7
275.3	Disorders of Phosphorus Metabolism	5	11.4	1	2.9	3	7.7	9	7.7
276.2	Acidosis	0	0.0	0	0.0	2	5.2	2	1.7
276.3	Alkalosis	2	4.6	0	0.0	1	2.6	3	2.6
276.9	Electrolyte and Fluid Disorders, NEC	0	0.0	1	2.9	1	2.6	2	1.7
277.0	Cystic Fibrosis	80	182.9	105	304.6	87	224.4	272	232.5
277.5	Mucopolysaccharidosis	8	18.3	11	31.9	2	5.2	21	18.0
277.6	Other Deficiencies of Circulating Enzymes	0	0.0	0	0.0	4	10.3	4	3.4
277.8	Other Disorders of Metabolism	0	0.0	0	0.0	1	2.6	1	0.9
277.9	Unspecified Disorders of Metabolism	0	0.0	0	0.0	1	2.6	1	0.9
279.0	Deficiency of Humoral Immunity	4	9.1	12	34.8	4	10.3	20	17.1
279.1	Deficiency of Cell-Mediated Immunity	0	0.0	0	0.0	1	2.6	1	0.9
279.2	Combined Immunity Deficiency	0	0.0	0	0.0	2	5.2	2	1.7
282.4	Thalassaemias	15	34.3	7	20.3	16	41.3	38	32.5
282.9	Unspecified Hereditary Haemolytic Anaemias	0	0.0	1	2.9	0	0.0	1	0.9
284.0	Constitutional Aplastic Anaemia	2	4.6	1	2.9	4	10.3	7	6.0
285.8	Other Specified Anaemias	1	2.3	0	0.0	0	0.0	1	0.9
286.2	Congenital Factor XI Deficiency	2	4.6	0	0.0	1	2.6	3	2.6
286.3	Congenital Deficiency of Other Clotting Factors	0	0.0	0	0.0	1	2.6	1	0.9
287.3	Primary Thrombocytopenia	0	0.0	0	0.0	1	2.6	1	0.9
287.5	Thrombocytopenia, Unspecified	0	0.0	0	0.0	1	2.6	1	0.9
288.0	Agranulocytosis	0	0.0	0	0.0	1	2.6	1	0.9
288.1	Funct Disorders of Neutrophil Polymorphs	0	0.0	0	0.0	1	2.6	1	0.9

Table A2.3
(continued)

Table A 2.3

Recessive conditions.....continued

*Indicates special Registry code (see Appendix 1, Table A 1.7)

ICD9	RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
289.8	Other Dis of Blood and Blood-Forming Organs	0	0.0	1	2.9	1	2.6	2	1.7
318.1	Severe Mental Retardation	2	4.6	1	2.9	0	0.0	3	2.6
318.2	Profound Mental Retardation	0	0.0	1	2.9	0	0.0	1	0.9
319	Unspecified Mental Retardation	0	0.0	3	8.7	0	0.0	3	2.6
330.0	Leucodystrophy	2	4.6	6	17.4	2	5.2	10	8.5
330.1	Cerebral Lipidoses	5	11.4	10	29.0	3	7.7	18	15.4
330.8	Other Cerebral Degenerations in Childhood	2	4.6	1	2.9	6	15.5	9	7.7
334.0	Friedreich's Ataxia	8	18.3	0	0.0	0	0.0	8	6.8
334.1	Hereditary Spastic Paraplegia	3	6.9	2	5.8	2	5.2	7	6.0
334.8	Other Spino-Cerebellar Diseases	1	2.3	2	5.8	0	0.0	3	2.6
335.0	Werdnig-Hoffmann Disease	6	13.7	19	55.1	15	38.7	40	34.2
335.1	Spinal Muscular Atrophy	2	4.6	1	2.9	2	5.2	5	4.3
335.9	Unspecified Anterior Horn Cell Disease	0	0.0	0	0.0	1	2.6	1	0.9
343.9	Unspecified Infantile Cerebral Palsy	0	0.0	1	2.9	0	0.0	1	0.9
345.7*	Epilepsia Partialis Continua	0	0.0	1	2.9	0	0.0	1	0.9
349.8	Other Disorders of Nervous System	3	6.9	1	2.9	0	0.0	4	3.4
356.1	Peroneal Muscular Atrophy	4	9.1	1	2.9	0	0.0	5	4.3
356.4	Idiopathic Progressive Polyneuropathy	1	2.3	1	2.9	0	0.0	2	1.7
358.8*	Other Myoneural Disorders	18	41.1	4	11.6	0	0.0	22	18.8
359.1	Hereditary Progressive Muscular Dystrophy	19	43.4	3	8.7	0	0.0	22	18.8
359.9	Unspecified Muscular Dystrophyies	1	2.3	0	0.0	0	0.0	1	0.9
360.3	Hypotony of Eye	0	0.0	0	0.0	1	2.6	1	0.9
362.1	Other B'ground Retinopathy & Ret Vasc Changes	0	0.0	0	0.0	1	2.6	1	0.9
362.7	Hereditary Retinal Dystrophies	21	48.0	10	29.0	0	0.0	31	26.5
368.5	Colour Vision Deficiences	1	2.3	0	0.0	0	0.0	1	0.9

Table A2.3 (continued)

Table A 2.3

Recessive conditions.....continued

*Indicates special Registry code (see Appendix 1, Table A 1.7)

ICD9	RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
369.0	Blindness, Both Eyes	1	2.3	1	2.9	1	2.6	3	2.6
369.9	Unspecified Visual Loss	0	0.0	0	0.0	1	2.6	1	0.9
377.1	Optic Atrophy	2	4.6	0	0.0	0	0.0	2	1.7
379.5	Nystagmus and Other Irregular Eye Movements	2	4.6	1	2.9	1	2.6	4	3.4
389.1	Sensorineural Deafness	9	20.6	12	34.8	8	20.6	29	24.8
389.7	Deaf Mutism, Not Elsewhere Specified	1	2.3	0	0.0	0	0.0	1	0.9
389.9*	Unspecified Deafness	20	45.7	12	34.8	4	10.3	36	30.8
425.3	Endocardial Fibroelastosis	0	0.0	0	0.0	1	2.6	1	0.9
448.0	Hereditary Haemorrhagic Telangiectasia	0	0.0	0	0.0	1	2.6	1	0.9
523.5	Periodontosis	1	2.3	0	0.0	0	0.0	1	0.9
572.3	Portal Hypertension	0	0.0	0	0.0	2	5.2	2	1.7
581.9	Unspecified Nephrotic Syndrome	1	2.3	0	0.0	0	0.0	1	0.9
585	Chronic Renal Failure	2	4.6	0	0.0	0	0.0	2	1.7
588.8	Other Dis Resulting fr Impaired Renal Function	0	0.0	1	2.9	0	0.0	1	0.9
742.1	Microcephalus	5	11.4	4	11.6	1	2.6	10	8.5
742.2	Reduction Deformities of Brain	0	0.0	0	0.0	2	5.2	2	1.7
742.3	Congenital Hydrocephalus	0	0.0	2	5.8	3	7.7	5	4.3
742.8	Other Specified Anomalies of Nervous System	1	2.3	0	0.0	0	0.0	1	0.9
743.1	Microphthalmos	0	0.0	0	0.0	1	2.6	1	0.9
743.2	Buphthalmos	7	16.0	7	20.3	3	7.7	17	14.5
743.3	Congenital Cataract and Lens Anomalies	3	6.9	2	5.8	0	0.0	5	4.3
745.4	Ventricular Septal Defect	0	0.0	1	2.9	1	2.6	2	1.7
746.2	Ebstein's Anomaly	0	0.0	0	0.0	1	2.6	1	0.9
746.8	Other Specified Anomalies of Heart	0	0.0	0	0.0	1	2.6	1	0.9
747.9	Unspecified Anomalies of Circulatory System	0	0.0	1	2.9	0	0.0	1	0.9

Table A2.3 (continued)

Table A 2.3

Recessive conditions.....continued

*Indicates special Registry code (see Appendix 1, Table A 1.7)

ICD9	RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
751.3	Hirschspsr Dis & Other Congen Func. Dis of Colon	0	0.0	0	0.0	1	2.6	1	0.9
751.6	Anomalies of Gallbladder, Bile Ducts and Liver	0	0.0	1	2.9	0	0.0	1	0.9
752.7	Indeterminate Sex and Pseudohermaphroditism	1	2.3	4	11.6	0	0.0	5	4.3
753.0	Renal Agenesis and Dysgenesis	0	0.0	5	14.5	1	2.6	6	5.1
753.1	Cystic Kidney Disease	11	25.1	10	29.0	7	18.1	28	23.9
754.7*	Clubfoot	0	0.0	0	0.0	1	2.6	1	0.9
755.2	Reduction Deformities of Upper Limb	0	0.0	0	0.0	1	2.6	1	0.9
755.8	Other Specified Anomalies of Unspecified Limb	0	0.0	0	0.0	3	7.7	3	2.6
756.0*	Anomalies of Skull and Face Bones	0	0.0	0	0.0	1	2.6	1	0.9
756.4	Chondrodystrophy	2	4.6	2	5.8	5	12.9	9	7.7
756.5	Osteodystrophies	1	2.3	8	23.2	7	18.1	16	13.7
756.6	Anomalies of Diaphragm	0	0.0	1	2.9	1	2.6	2	1.7
756.8	Other Spec Anom of Muscle, Tendon, Fascia, etc.	1	2.3	0	0.0	1	2.6	2	1.7
757.1	Ichthyosis Congenita	2	4.6	0	0.0	4	10.3	6	5.1
757.2	Dermatoglyphic Anomalies	1	2.3	0	0.0	0	0.0	1	0.9
757.3*	Other Specified Anomalies of Skin	8	18.3	5	14.5	1	2.6	14	12.0
757.8	Other Specified Anomalies of the Integument	1	2.3	0	0.0	0	0.0	1	0.9
759.0	Anomalies of Spleen	0	0.0	0	0.0	4	10.3	4	3.4
759.3	Situs Inversus	1	2.3	0	0.0	0	0.0	1	0.9
759.6	Other Hamartoses Not Elsewhere Classified	0	0.0	0	0.0	2	5.2	2	1.7
759.8	Other Specified Anomalies	7	16.0	18	52.2	21	54.2	46	39.3
783.4	Lack of Expected Normal Physiol Development	0	0.0	0	0.0	1	2.6	1	0.9
TOTAL		401	916.6	406	1178.0	372	959.5	1179	1007.8
SUM OF HIGHEST INDIVIDUAL RATES									1655.3

Table A2.3 (continued)

Table A 2.4

Complete tabulation of X-linked conditions by birth-year ranges

* Indicates special Registry code (see Appendix 1, Table A 1.7)

ICD9	X-LINKED CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
257.8	Other Testicular Dysfunction	8	18.3	0	0.0	7	18.1	15	12.8
270.6	Disorders of Urea Cycle Metabolism	1	2.3	0	0.0	3	7.7	4	3.4
275.4	Disorders of Calcium Metabolism	0	0.0	2	5.8	0	0.0	2	1.7
277.5	Mucopolysaccharidosis	3	6.9	3	8.7	0	0.0	6	5.1
279.0	Deficiency of Humoral Immunity	6	13.7	2	5.8	0	0.0	8	6.8
279.1	Deficiency of Cell-Mediated Immunity	0	0.0	1	2.9	1	2.6	2	1.7
279.2	Combined Immunity Deficiency	0	0.0	1	2.9	0	0.0	1	0.9
282.2	Anaemia Due to Dis of Gluthathione Metab	3	6.9	2	5.8	14	36.1	19	16.2
286.0	Congenital Factor VIII Disorder	28	64.0	24	69.6	14	36.1	66	56.4
286.1	Congenital Factor IX Disorder	7	16.0	10	29.0	1	2.6	18	15.4
286.9	Other and Unspecified Coagulation Defects	1	2.3	0	0.0	0	0.0	1	0.9
288.1	Functional Disorders of Neutrophil Polymorphs	0	0.0	0	0.0	3	7.7	3	2.6
317.1*	Borderline Mental Retardation	2	4.6	0	0.0	1	2.6	3	2.6
317.2*	Mild Mental Retardation	3	6.9	1	2.9	0	0.0	4	3.4
318.0	Moderate Mental Retardation	4	9.1	1	2.9	0	0.0	5	4.3
318.1	Severe Mental Retardation	2	4.6	0	0.0	0	0.0	2	1.7
318.2	Profound Mental Retardation	1	2.3	2	5.8	0	0.0	3	2.6
319	Unspecified Mental Retardation	1	2.3	1	2.9	4	10.3	6	5.1
330.0	Leucodystrophy	0	0.0	0	0.0	1	2.6	1	0.9
359.0	Congenital Hereditary Muscular Dystrophy	0	0.0	0	0.0	1	2.6	1	0.9
359.1	Hereditary Progressive Muscular Dystrophy	43	98.3	34	98.6	13	33.5	90	76.9
362.7	Hereditary Retinal Dystrophies	1	2.3	1	2.9	1	2.6	3	2.6
366.4	Cataract Associated with Other Disorders	0	0.0	0	0.0	1	2.6	1	0.9
368.4	Visual Field Defects	0	0.0	0	0.0	1	2.6	1	0.9
368.5	Colour Vision Deficiencies	29	66.3	32	92.8	14	36.1	75	64.1

Table A 2.4

X-linked conditions.....continued

*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD9	X-LINKED CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
377.1	Optic Atrophy	1	2.3	0	0.0	0	0.0	1	0.9
379.5	Nystagmus and Other Irregular Eye Movements	0	0.0	0	0.0	1	2.6	1	0.9
588.1	Nephrogenic Diabetes Insipidus	3	6.9	2	5.8	4	10.3	9	7.7
742.2	Reduction Deformities of Brain	0	0.0	1	2.9	1	2.6	2	1.7
742.3	Congenital Hydrocephalus	0	0.0	1	2.9	0	0.0	1	0.9
743.5	Congenital Anomalies of Posterior Segment	2	4.6	2	5.8	3	7.7	7	6.0
743.8*	Other Specified Anomalies of Eye	1	2.3	2	5.8	2	5.2	5	4.3
752.6	Hypospadias and Epispadias	0	0.0	1	2.9	0	0.0	1	0.9
752.7	Indetermin Sex and Pseudohermaphroditism	0	0.0	1	2.9	0	0.0	1	0.9
755.2	Reduction Deformities of Upper Limb	1	2.3	0	0.0	0	0.0	1	0.9
756.0*	Anomalies of Skull and Face Bones	2	4.6	1	2.9	3	7.7	6	5.1
757.1	Ichthyosis Congenita	0	0.0	0	0.0	1	2.6	1	0.9
757.2	Dermatoglyphic Anomalies	0	0.0	1	2.9	0	0.0	1	0.9
757.3*	Other Specified Anomalies of Skin	3	6.9	3	8.7	7	18.1	13	11.1
759.8	Other Specified Congenital Anomalies	1	2.3	0	0.0	3	7.7	4	3.4
TOTAL		157	358.9	132	383.0	105	270.8	394	336.8
SUM OF HIGHEST INDIVIDUAL RATES									532.4

Table A2.4
(continued)

APPENDIX 3

Detailed tables of congenital anomalies previously identified in Chapters 3, 4 and 5, and discussed in Chapter 6.

These tables have been extracted from earlier tables and are restricted to conditions listed in the "Congenital Anomalies" section of the International Classification of Diseases (9th Revision), rubrics 740.0 through 759.9.

Table A3.1 Dominant

Table A3.2 Recessive

Table A3.3 X-linked

Table A3.4 Autosomal chromosome

Table A3.5 Sex chromosome

Table A3.6 Multifactorial

Table A 3.1

Dominant conditions with ICD codes 740-759

*Indicates special Registry code (see Appendix 1, Table A1.7)

CONGENITAL ANOMALIES		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9	DOMINANT CONDITIONS	N	Rate	N	Rate	N	Rate	N	Rate
742.3	Congenital Hydrocephalus	0	0.0	1	2.9	0	0.0	1	0.9
742.4	Other Specified Anomalies of Brain	0	0.0	1	2.9	4	10.3	5	4.3
743.2	Buphthalmos	1	2.3	0	0.0	0	0.0	1	0.9
743.3	Congenital Cataract and Lens Anomalies	21	48.0	10	29.0	5	12.9	36	30.8
743.4	Coloboma and Other Anom of Ant Seg	5	11.4	3	8.7	4	10.3	12	10.3
743.5	Congenital Anomalies of Posterior Segment	1	2.3	0	0.0	1	2.6	2	1.7
743.6	Congen Anom of Eyelids, Lac System and Orbit	0	0.0	5	14.5	2	5.2	7	6.0
743.9	Unspecified Anomalies of Eye	0	0.0	0	0.0	1	2.6	1	0.9
744.2	Other Specified Anomalies of Ear	0	0.0	0	0.0	1	2.6	1	0.9
746.8	Other Specified Anomalies of Heart	1	2.3	0	0.0	0	0.0	1	0.9
747.0	Patent Ductus Arteriosus	0	0.0	0	0.0	1	2.6	1	0.9
749.2	Cleft Palate with Cleft Lip	0	0.0	3	8.7	1	2.6	4	3.4
752.4	Anom of Cervix, Vagina and Extern F Gen	0	0.0	0	0.0	1	2.6	1	0.9
752.6	Hypospadias and Epispadias	0	0.0	2	5.8	2	5.2	4	3.4
753.1	Cystic Kidney Disease	2	4.6	4	11.6	3	7.7	9	7.7
755.0	Polydactyly	6	13.7	16	46.4	14	36.1	36	30.8
755.1*	Syndactyly	0	0.0	1	2.9	4	10.3	5	4.3
755.2	Reduction Deformaties of Upper Limb	1	2.3	4	11.6	6	15.5	11	9.4
755.3	Reduction Deformaties of Lower Limb	1	2.3	1	2.9	0	0.0	2	1.7
755.5*	Other Anom of Upper Limb, Inc Shoulder Girdle	3	6.9	2	5.8	9	23.2	14	12.0
755.8	Other Specified Anomalies of Unspecified Limb	2	4.6	4	11.6	1	2.6	7	6.0
756.0*	Anomalies of Skull and Face Bones	9	20.6	11	31.9	14	36.1	34	29.1
756.1	Anomalies of Spine	6	13.7	3	8.7	1	2.6	10	8.5
756.4	Chondrodystrophy	48	109.7	21	60.9	20	51.6	89	76.1
756.5	Osteodystrophies	24	54.9	31	89.9	29	74.8	84	71.8

Table A 3.1

Dominant conditions, ICD 740-759 .....continued

CONGENITAL ANOMALIES		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9	DOMINANT CONDITIONS	N	Rate	N	Rate	N	Rate	N	Rate
756.8	Other Spec Anom of Muscle, Tendon, Fascia, etc.	13	29.7	14	40.6	7	18.1	34	29.1
756.9	Unspec Anomalies of Musculoskeletal Syst	2	4.6	8	23.2	0	0.0	10	8.5
757.0	Hereditary Oedema of Legs	0	0.0	0	0.0	2	5.2	2	1.7
757.1	Ichthyosis Congenita	0	0.0	1	2.9	3	7.7	4	3.4
757.3*	Other Specified Congenital Anomalies of Skin	11	25.1	5	14.5	6	15.5	22	18.8
759.5	Tuberous Sclerosis	13	29.7	23	66.7	22	56.7	58	49.6
759.6	Other Congenital Hamartoses (N.E.C.)	7	16.0	1	2.9	3	7.7	11	9.4
759.7	Multiple Congenital Anomalies, So Described	8	18.3	7	20.3	5	12.9	20	17.1
759.8	Other Specified Congenital Anomalies	17	38.9	16	46.4	9	23.2	42	35.9
TOTAL		202	461.7	198	574.5	181	466.8	581	496.6
SUM OF HIGHEST INDIVIDUAL RATES									741.5

Table A3.1
(continued)

Table A 3.2

Recessive conditions with ICD codes 740-759

ICD9	CONGENITAL ANOMALIES RECESSIVE CONDITIONS	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
		N	Rate	N	Rate	N	Rate	N	Rate
742.1	Microcephalus	5	11.4	4	11.6	1	2.6	10	8.5
742.2	Reduction Deformities of Brain	0	0.0	0	0.0	2	5.2	2	1.7
742.3	Congenital Hydrocephalus	0	0.0	2	5.8	3	7.7	5	4.3
742.8	Other Specified Anomalies of Nervous System	1	2.3	0	0.0	0	0.0	1	0.9
743.1	Microphthalmos	0	0.0	0	0.0	1	2.6	1	0.9
743.2	Buphthalmos	7	16.0	7	20.3	3	7.7	17	14.5
743.3	Congenital Cataract and Lens Anomalies	3	6.9	2	5.8	0	0.0	5	4.3
745.4	Ventricular Septal Defect	0	0.0	1	2.9	1	2.6	2	1.7
746.2	Ebstein's Anomaly	0	0.0	0	0.0	1	2.6	1	0.9
746.8	Other Specified Anomalies of Heart	0	0.0	0	0.0	1	2.6	1	0.9
747.9	Unspecified Anomalies of Circulatory System	0	0.0	1	2.9	0	0.0	1	0.9
751.3	Hirschspsr Dis. & Other Congen Func. Dis of Colon	0	0.0	0	0.0	1	2.6	1	0.9
751.6	Anomalies of Gallbladder, Bile Ducts and Liver	0	0.0	1	2.9	0	0.0	1	0.9
752.7	Indeterminate Sex and Pseudohermaphroditism	1	2.3	4	11.6	0	0.0	5	4.3
753.0	Renal Agenesis and Dysgenesis	0	0.0	5	14.5	1	2.6	6	5.1
753.1	Cystic Kidney Disease	11	25.1	10	29.0	7	18.1	28	23.9
754.7*	Clubfoot	0	0.0	0	0.0	1	2.6	1	0.9
755.2	Reduction Deformities of Upper Limb	0	0.0	0	0.0	1	2.6	1	0.9
755.8	Other Spec Anomalies of Unspecified Limb	0	0.0	0	0.0	3	7.7	3	2.6
756.0*	Anomalies of Skull and Face Bones	0	0.0	0	0.0	1	2.6	1	0.9
756.4	Chondrodystrophy	2	4.6	2	5.8	5	12.9	9	7.7
756.5	Osteodystrophies	1	2.3	8	23.2	7	18.1	16	13.7
756.6	Anomalies of Diaphragm	0	0.0	1	2.9	1	2.6	2	1.7
756.8	Other Spec Anom of Muscle, Tendon, Fascia, etc.	1	2.3	0	0.0	1	2.6	2	1.7
757.1	Ichthyosis Congenita	2	4.6	0	0.0	4	10.3	6	5.1

Table A 3.2

Recessive conditions, ICD 740-759.....continued

CONGENITAL ANOMALIES		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9	RECESSIVE CONDITIONS	N	Rate	N	Rate	N	Rate	N	Rate
757.2	Dermatoglyphic Anomalies	1	2.3	0	0.0	0	0.0	1	0.9
757.3*	Other Spec Congen Anomalies of Skin	8	18.3	5	14.5	1	2.6	14	12.0
757.8	Other Specified Anomalies of the Integument	1	2.3	0	0.0	0	0.0	1	0.9
759.0	Anomalies of Spleen	0	0.0	0	0.0	4	10.3	4	3.4
759.3	Situs Inversus	1	2.3	0	0.0	0	0.0	1	0.9
759.6	Other Congenital Hamartoses (N.E.C.)	0	0.0	0	0.0	2	5.2	2	1.7
759.8	Other Specified Congenital Anomalies	7	16.0	18	52.2	21	54.2	46	39.3
TOTAL		52	118.9	71	206.0	74	190.9	197	168.4
SUM OF HIGHEST INDIVIDUAL RATES									290.3

Table A3.2
(continued

Table A 3.3

X-linked conditions with ICD codes 740-759

*Indicates special Registry code (see Appendix 1, Table A 1.7)

CONGENITAL ANOMALIES		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9	X-LINKED CONDITIONS	N	Rate	N	Rate	N	Rate	N	Rate
742.2	Reduction Deformities of Brain	0	0.0	1	2.9	1	2.6	2	1.7
742.3	Congenital Hydrocephalus	0	0.0	1	2.9	0	0.0	1	0.9
743.5	Congenital Anomalies of Posterior Segment	2	4.6	2	5.8	3	7.7	7	6.0
743.8*	Other Specified Anomalies of Eye	1	2.3	2	5.8	2	5.2	5	4.3
752.6	Hypospadias and Epispadias	0	0.0	1	2.9	0	0.0	1	0.9
752.7	Indeterm Sex and Pseudohermaphroditism	0	0.0	1	2.9	0	0.0	1	0.9
755.2	Reduction Deformities of Upper Limb	1	2.3	0	0.0	0	0.0	1	0.9
756.0*	Anomalies of Skull and Face Bones	2	4.6	1	2.9	3	7.7	6	5.1
757.1	Ichthyosis Congenita	0	0.0	0	0.0	1	2.6	1	0.9
757.2	Dermatoglyphic Anomalies	0	0.0	1	2.9	0	0.0	1	0.9
757.3*	Other Specified Congenital Anomalies of Skin	3	6.9	3	8.7	7	18.1	13	11.1
759.8	Other Specified Congenital Anomalies	1	2.3	0	0.0	3	7.7	4	3.4
TOTAL		10	22.9	13	37.7	20	51.6	43	36.8
SUM OF HIGHEST INDIVIDUAL RATES									66.4

Table A 3.4

Autosomal Chromosome conditions with ICD codes 740-759

*Indicates special Registry code (see Appendix 1, Table A 1.7)

CONGENITAL ANOMALIES		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9	AUTOSOMAL CHROMOSOME CONDITIONS	N	Rate	N	Rate	N	Rate	N	Rate
758.0	Down's Syndrome	571	1305.1	460	1334.6	394	1016.2	1425	1218.1
758.1	Patau's Syndrome	3	6.9	15	43.5	22	56.7	40	34.2
758.2	Edward's Syndrome	1	2.3	31	89.9	57	147.0	89	76.1
758.3	Autosomal Deletion Syndromes	4	9.1	4	11.6	26	67.1	34	29.1
758.4	Bal Autosomal Translocation in Normal	11	25.1	5	14.5	5	12.9	21	18.0
758.5	Other Conditions Due to Autosomal Anomalies	6	13.7	14	40.6	31	80.0	51	43.6
758.9	Anomaly of Unspecified Chromosome	1	2.3	0	0.0	3	7.7	4	3.4
TOTAL		597	1364.6	529	1534.8	538	1387.7	1664	1422.4
SUM OF HIGHEST INDIVIDUAL RATES									1718.3

Table A 3.5

Sex Chromosomal conditions with ICD codes 740-759

*Indicates special Registry code (see Appendix 1, Table A 1.7)

CONGENITAL ANOMALIES		COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
		1952-63		1964-73		1974-83		TOTAL	
ICD9	SEX CHROMOSOMAL CONDITIONS	N	Rate	N	Rate	N	Rate	N	Rate
758.6	Gonadal Dysgenesis	33	75.4	26	75.4	23	59.3	82	70.1
758.7	Klinefelter's Syndrome	28	64.0	11	31.9	5	12.9	44	37.6
758.8	Other Conditions Due to Sex Chromosome	3	6.9	2	5.8	5	12.9	10	8.5
TOTAL		64	146.3	39	113.2	33	85.1	136	116.3
SUM OF HIGHEST INDIVIDUAL RATES									152.3

Table A 3.6

Multifactorial conditions with ICD codes 740-759

*Indicates special Registry code (see Appendix 1, Table A1.7)

CONGENITAL ANOMALIES		PERIOD OF	MINIMUM (Single diag.)		ADDITIONAL (2 or more diag.)		EXPANDED MINIMUM	
ICD9	MULTIFACTORIAL CONDITIONS	CHOICE	N	Rate	N	Rate	N	Rate
740	Anencephaly	1974-83	50	129.0	9	23.2	59	152.2
741	Spina Bifida	1974-83	67	172.8	11	28.4	78	201.2
742	Encephalocele	1974-83	8	20.6	2	5.2	10	25.8
742.3	Congenital Hydrocephalus	1964-73	99	287.2	25	72.5	124	359.8
745-7	Congen Anom of Heart & Circ System	1964-73	1699	4929.4	30	87.0	1729	5016.5
749	Cleft Palate & Cleft Lip	1964-73	463	1343.3	45	130.6	508	1473.9
750.5	Con Hypertropic Pyloric Stenosis	1974-83	909	2344.6	8	20.6	917	2365.2
751.3	Hirschsprung's Diseases etc.	1964-73	60	174.1	4	11.6	64	185.7
752.6	Hypospadias and Epispadias	1964-73	558	1619.0	70	203.1	628	1822.1
754.7*	Clubfoot	1974-83	1967	5073.4	16	41.3	1983	5114.7
754.3	Congenital Dislocation of Hip	1974-83	1322	3409.8	11	28.4	1333	3438.2
754.9*	Congenital Dislocatable Hip	1974-83	622	1604.3	12	31.0	634	1635.3
TOTAL			7824	21107.6	243	682.8	8067	21790.4
Adjusted Total**								23076.0

** Adjusted to allow for double etc multifactorial diagnoses (see text, p.36)

Table A 3.7

Cases with a Registry etiology code of "01" (Genetic: unknown etiology), after removing those with a diagnosis of strabismus (ICD 378).

CONGENITAL ANOMALIES	COUNTS AND RATES (per million live births) BY BIRTH YEAR RANGE							
	1952-63		1964-73		1974-83		TOTAL	
GENETIC UNKNOWN	N	Rate	N	Rate	N	Rate	N	Rate
Single Diagnosis	469	1072.0	294	853.0	155	399.8	918	784.7
Multiple Diagnoses	234	534.9	122	354.0	88	277.0	444	379.5
TOTAL	703	1606.9	416	1207.0	243	626.8	1362	1164.2

APPENDIX 4 Mental retardation (ICD 317-319)

Cases of mental retardation (MR) have been counted under various etiological headings in previous chapters. These figures are summarized in Table A4.1.

The total shown in Table A4.1 is an underestimate of the true frequency of MR for two main reasons: (i) many cases with MR are coded to a diagnostic code that is outside the range ICD 317-319, because the MR is part of a syndrome (e.g. Down syndrome, ICD 758.0), and (ii) only "borderline" and "mild" MR were included in the 22 selected multifactorial diagnoses.

A more complete view of the MR problem is therefore provided by the accompanying tables A4.2-5, which show a peak rate in the first decade of 9734.8 p.m.l.b. This figure is unchanged if peak rates for individual diagnoses are considered, since they all occurred in the 1952-63 birth period.

In terms of the etiology assigned to these cases routinely by the Registry, in the 1952-63 period (Table A4.3), 63% were of unknown etiology and 14% were associated with Autosomal chromosome abnormalities.

Note that in Tables A4.2-5, diagnoses have been counted, but this is the same as counting cases, because each category is mutually exclusive. (This is in contrast to the situation in Tables 6.3 to 6.5 where some cases had more than one diagnosis).

Table A4.1 Mental Retardation: Summary of highest rates from earlier chapters.

Table A4.2 Mental Retardation: Total cases in Registry, by severity, and by birth periods.

Table A4.3 Mental Retardation: By severity and coded etiology, 1952-1963.

Table A4.4 Mental Retardation: By severity and coded etiology, 1964-1973.

Table A4.5 Mental Retardation: By severity and coded etiology, 1974-1983.

Table A 4.1

Mental Retardation: Summary of highest rates (per million live births) from earlier chapters
*Indicates special Registry code (see Appendix 1, Table A1.7)

	Dom	Rec	X-linked	Auto Ch	Sex Ch	Multi factorial	Total
317.1*	0	0	4.6	0	0	941.7	946.3
317.2*	0	0	6.9	0	0	592.0	598.9
318.0	0	0	9.1	0	0	0	9.1
318.1	0	4.6	4.6	0	0	0	9.2
318.2	0	2.9	5.8	0	0	0	8.7
319	2.9	8.7	10.3	0	0	0	21.9
Total	2.9	16.2	41.3	0	0	1533.7	1594.1

Table A 4.2

Mental Retardation: Total cases (per million live births) in Registry, by severity, and by birth period

*Indicates special Registry code (see Appendix 1, Table A1.7)

ICD	Severity	1952-63		1964-73		1974-83		Total	
		N	Rate	N	Rate	N	Rate	N	Rate
317.1*	Borderline	1102	2518.8	268	777.6	21	54.2	1391	1189.0
317.2*	Mild	815	1862.8	280	812.4	46	118.6	1141	975.3
318.0	Moderate	546	1248.0	216	626.7	39	100.6	801	684.7
318.1	Severe	338	772.6	191	554.2	65	167.7	594	507.7
318.2	Profound	405	925.7	186	539.7	15	38.7	606	518.0
319	Unspecified	1052	2404.6	768	2228.3	740	1908.7	2560	2188.3
	Total	4258	9732.5	1909	5538.7	926	2388.4	7093	6063.1

Table A 4.3

Mental Retardation: By severity and coded etiology, 1952-1963
*Indicates special Registry code (see Appendix 1, Table A1.7)

		Genetic							Other			
ICD	Severity	Dom	Rec	X-link	Auto Chrom	Sex Chrom	Multi-Fact	Unspec Genetic	Cong Anom	Perinatal etc.	Etiol Unknown	Total
317.1*	Borderline	6	2	7	4	1	0	40	65	83	894	1102
317.2*	Mild	3	6	5	38	3	2	42	72	51	593	815
318.0	Moderate	2	11	4	110	2	0	24	36	42	42	546
318.1	Severe	2	8	3	77	0	1	8	35	24	180	338
318.2	Profound	4	12	2	46	0	1	14	78	40	208	405
319	Unspecified	5	15	5	302	5	3	25	124	68	500	1052
	Total	22	54	26	577	11	7	153	410	308	2690	4258

Table A 4.4

Mental Retardation: By severity and coded etiology, 1964-1973

*Indicates special Registry code (see Appendix 1, Table A1.7)

		Genetic							Other			
ICD	Severity	Dom	Rec	X-link	Auto Chrom	Sex Chrom	Multi-Fact	Unspec Genetic	Cong Anom	Perinatal etc.	Etiol Unknown	Total
317.1*	Borderline	3	1	1	7	1	0	4	18	16	217	268
317.2*	Mild	3	0	3	34	1	0	3	28	19	189	280
318.0	Moderate	3	4	2	63	1	1	5	22	20	95	216
318.1	Severe	3	7	1	27	0	1	8	45	14	85	191
318.2	Profound	3	6	2	12	0	0	2	56	23	82	186
319	Unspecified	11	15	1	337	1	0	10	85	34	274	768
	Total	26	33	10	480	4	2	32	254	126	942	1909

Table A 4.5

Mental Retardation: By severity and coded etiology, 1974-1983

*Indicates special Registry code (see Appendix 1, Table A1.7)

		Genetic							Other			
ICD	Severity	Dom	Rec	X-link	Auto Chrom	Sex Chrom	Multi-Fact	Unspec Genetic	Cong Anom	Perinatal etc.	Etiol Unknown	Total
317.1*	Borderline	2	0	1	1	0	1	2	5	2	7	21
317.2*	Mild	2	2	0	8	0	0	4	5	3	22	46
318.0	Moderate	1	0	0	4	0	0	1	14	6	13	39
318.1	Severe	0	1	1	5	0	0	1	16	8	33	65
318.2	Profound	0	1	1	1	0	0	0	7	1	4	15
319	Unspecified	6	3	6	429	0	2	3	127	38	126	740
	Total	11	7	9	448	0	3	11	174	58	205	926